"I would have everie man write what he knowes and no more."—MONTAIGNE

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EDITORIAL

AN IMPORTANT JUDGMENT

"PHYSICIANS of all men are most happy; whatever good success they have the world proclaimeth, and what faults they commit the earth covereth." So wrote Francis Quarles in the "Hieroglyphickes of the Life of Man" in 1638. However true this might have been in the seventeenth century, it is certainly less than the truth in the second half of the twentieth. "What faults they commit", are in these days all too likely to be displayed naked and ashamed in a court of law. A year or so ago legal proceedings between patients and doctors or patients and hospital boards were assuming an importance sufficient to provoke more than one responsible and authoritative warning that the correct treatment of the patient was being endangered by fear of litigation. One suspects that recently there is some easement of the situation, because the general public has been made aware that "accidental" is not always synonymous with "negligent".

The case, tried at the Liverpool Court of Passage on December 19 last, should help many physicians, especially anaesthetists, to control the intention tremor which may have developed during recent months, when making intravenous injections. The aetiology of this tremor has been apprehension, conscious or subconscious, regarding possible consequences of this everyday and routine procedure.

In this action Mrs. C. P. alleged that Dr. I. P. C., a House Physician, had been negligent in the performance of an injection of Ferrivenin in June 1952 and claimed damages from the doctor and from the Hospital Management Committee.

The plaintiff, a married woman aged 53, was being treated as an inpatient for anaemia and on three previous occasions Dr. I. P. C. had successfully injected Ferrivenin into a vein of the anticubital fossa of the right arm. On the fourth occasion a small quantity of the substance entered the tissues surrounding the vein, causing an abscess to develop which subsequently required the patient's readmission to hospital for treatment.

In her evidence, the plaintiff said that at the beginning of the injection she had felt a terrible pain in her arm and that Dr. I. P. C. had persisted in the injection despite her continued complaints of pain. Crossexamined by Miss Rose Heilbron, Q.C., instructed by Messrs Hempsons, solicitors acting for the Medical Defence Union, the plaintiff said that she had not watched the injection nor had she seen what the doctor was doing. She based her allegation on the fact that when she complained of pain Dr. I. P. C. had said "I'll have to let the whole lot go now."

Dr. I. P. C. gave evidence describing the technique he had employed and said that on this occasion the patient complained of pain after he had injected about 1 ml. He had realized that the point of the needle had come out of the vein and at once withdrew the needle and ordered poultices to be applied to the arm.

An expert witness for the plaintiff said that he had given over 120,000 intravenous injections but had never had a case where an adverse reaction had occurred. He agreed that extravenous injection could occur even if good care was taken.

Expert evidence was given by the defence that it was not always easy to ensure that the point of the needle remained in the vein and that the escape of the irritant solution into the surrounding tissues had happened on a number of occasions to practically everyone of experience.

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EFFECTS OF ANAESTHETIC AGENTS AND RELAXANTS ON VASCULAR TONE STUDIES IN SANDISON CLARK CHAMBERS

BY

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INTRODUCTION

THE effects on blood vessels of drugs commonly used in anaesthesia are of great interest to the clinician whose constant aim is to produce minimal physiological side effects during anaesthesia. A previous investigation using the Sandison Clark "*regenerated*" type chamber on the rabbit ear has been reported (Seldon et al., 1942). The present research has been carried out with the "*preformed*" ear chamber and in some cases the results differ from this earlier report.

In the preformed chamber the blood vessels under observation are the original subcutaneous vessels of the rabbit ear; in the regenerated type the blood vessels are the vessels formed in the process of repair.

It would appear more satisfactory to assess the effects of anaesthetic agents on the normally innervated vessels of the animal and not in those of the repair blastoma.

EAR CHAMBER DESIGN

The ear chamber used is of the conventional Sandison Clark type (Clark et al., 1930), with a raised table 6 mm in diameter, 1.5 mm high. However, it differs in that the tissue depth (200 μ in preformed chambers) is adjusted by the height of the outer pillars, and that the entire chamber is constructed from perspex, including the "cover glass". The use of a thick cover glass, makes the whole chamber very rigid, and yet provides adequate clearance for microscope objectives over the range of magnifications employed.

EAR CHAMBER INSERTION AND SUBSEQUENT EXAMINATION

The animals used are semi-lopeared adult rabbits, 2–4 kg in weight. The animals are housed in separate cages, in an environmental temperature of 70°F (±2°F) and fed on a standard diet (Bruce and Parkes No. 18).

Preformed ear chambers are inserted in each ear, using a sterile technique. At operation after reflection of the skin flaps, the central disc of cartilage is dissected away, leaving behind the outer perichondrum and overlying blood vessels, nerves and lymphatics. The ear chamber is inserted, the central table fitting the hole in the cartilage, and the other components are

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assembled and fixed into position. After operation, the animal is left for at least two weeks to allow for a completion of the demolition phase following injury, and a stabilization of the vascular bed. At the end of this period, the animal is trained to become accustomed to microscopic examination in the conscious state, using a rabbit holder which accommodates the animal in a sitting posture.

The animal is then ready for trials with pharmacological agents.

All experiments are carried out at constant room temperature (70°F) and constant conditions of illumination. Where possible the same chamber is used for multiple trials with different anaesthetics and drugs, allowing a suitable time interval for adequate recovery from each agent. This provides a uniformity of material, which minimizes idiosyncrasy and individual variation in behaviour, and also helps accustom the animal to anaesthetic procedures. The results recorded and illustrated in this paper are representative of the invariable effect produced by drugs. In occasional instances where it is considered that certain reactions are not due to the agent tested, but to complicating experimental factors (e.g. anoxia, nervous excitability), this is stated in the text.

The microscopic examination of the ear vessels is made on a "Holophot" photomicrographic unit, in which the ordinary quarter-plate camera is replaced with a 35-mm "Exacta" camera, enabling rapid repeated exposures, to record calibre changes in the vessels under observation. A vascular field is selected which contains a larger branching artery, and the changes in this vessel and the surrounding field are observed throughout a given trial. Whenever possible the same field is used for successive trials with various agents. After the ear chamber has been fixed to a specially designed stage applicator the animal is left to settle down, and several trial control exposures are made to record the "initial" tone or calibre of the vessels before proceeding to anaesthesia.

No attempt has been made to present the results quantitatively by measuring the size of the vessels. It is considered that this method is subject to an experimental error too large to permit quantitative assessment by measurement, of minute changes in vascular calibre which cannot be detected by ordinary visual examination of photographic records. Throughout an experiment, careful observations are made on the rate of blood flow in vessels, evidence of pulsation and the degree of vasomotion in arteries. In most experiments the changes in vascularity were also followed by simultaneous recording by a photo-electrical method from the opposite ear.

INTERPRETATION OF VASCULAR CALIBRE CHANGES IN EAR CHAMBERS

The Sandison Clark type ear chamber used in the experiments under consideration is of rigid construction. The tissues under observation cannot readily alter in total volume, and this factor profoundly influences the interpretation of the changes in the capillary bed observed when the volume of the layer contractile vessels alters with the exhibition of pharmacological agents. Active *arterial* and *arteriolar* contraction, brought about by a vasoconstrictor (e.g. adrenaline), is invariably accompanied by a compensatory dilatation of non-contractile small vessels (capillar-

ies and venules), the total vascular volume remaining relatively constant at the outset, until such time as transfer of liquid takes place from intravascular to extravascular spaces. The paradoxical behaviour of "rigid" tissues in respect of vascular calibre and blood flow, has been determined by Wright (1937), from experimental studies on the cranial contents.

The assumption that capillaries in the mammal behave passively, and do not possess the power of active muscular contractility, is still sub judice, although most investigators agree with this hypothesis (Clark and Clark, 1943; Chambers and Zweifach, 1947; Folkow, 1955). The behaviour of capillaries in rigid ear chambers, in response to vasotropic substances, also lends support to this view. It is considered that the term "capillary tone" should be rejected in favour of "capillary calibre". The term "tone" implies the presence of a tissue component which is actively contractile, i.e. a muscular tissue.

It follows that the observed changes in calibre of *capillaries*, *venules* and *veins*, in rigid ear chambers, must be interpreted with due attention to passive mechanical factors—a limitation reflected in other studies (Wilson, 1936; Levinson and Essex, 1943). This consideration particularly applies to the "preformed tissue" type chamber in which a much higher proportion of the total tissue volume consists of actively contractile vessels (arteries). The effects demonstrated in ear chambers on larger arteries and muscular arterioles are valid, but the reported effects on "non-contractile" vessels (capillaries and venules) cannot be regarded as representing the changes produced in the body.

Observations on the calibre of individual vessels in ear chambers in rabbits clearly indicate that it is impossible to define a "basal level of tone" for contractile vessels in these animals. In a trained animal, observed under apparently basal conditions in respect to environmental temperature, nervous excitability, posture, and illumination, the calibre of individual vessels of all sizes shows enormous variation. It is considered that interpretation of changes in calibre of a selected vessel (artery, arteriole or capillary) with the exhibition of a vasotropic agent, is completely unreliable unless gross pharmacodynamic changes are induced. Also, attempted quantitation of results by isolated measurements of vascular calibre, implies an experimental accuracy which does not exist. For this reason, studies of sizeable segments of larger arteries and the adjacent tissues, in thick preformed ear chambers, using lower powers of magnification, are preferable, and considered to provide much more consistent and useful information.

The confidence, expressed by Seldon et al. (1942), in a sampling technique which selects a single individual vessel for the interpretation of calibre changes, is not shared by the writers. It is also considered that the flexibility in the range of tone of peripheral arteries and arterioles, both general and local, in an animal under basal experimental conditions, together with the phenomena of phasic changes in tone—"vasomotion" (Clark and Clark, 1943; Wilson, 1936, 1953; Bozler, 1941, 1942, 1948; Evans and Schild, 1953)—makes an accurate assessment of "initial tone" subject to considerable error, particularly in anaesthetic experiments of relatively long

duration. In the experiments under consideration, the initial tone of vessels in a tissue field was assessed by observation and photography over a period prior to anaesthesia. All possible precautions were taken to ensure that the animal was trained for the experiment, and basal environmental conditions observed. Whilst the initial tone determined in this way was used as a yardstick for subsequent changes in calibre of vessels following anaesthesia, more confidence was placed in any changes in calibre which took place during the experiment as the plane of anaesthesia altered, or if relative anoxia or hypercarbia were induced. The conclusions at the end of this paper are based on an integration of all the observed changes, rather than on strict comparisons of vascular calibre before and after anaesthesia.

ILLUMINATION

Recent studies indicate that strong illumination causes a relaxation in the tone of vascular smooth muscle (Furchgott et al., 1955). The relaxation is enhanced by increasing the intensity of illumination and a loss of tone as high as 50 per cent may be induced. The peak range of the action spectrum responsible for this photodynamic effect in the rabbit is 365–370 mμ, disappearing below 340 mμ and above 450 mμ. The light source employed in the present experiments consists of a Pointolite lamp. The light is filtered with a Wratten green filter (58A, B2 Dark) in conjunction with a heat-resistant glass filter, giving a transmission spectrum of wavelength 480 mμ to 600 mμ, with the maximum transmission at 520 mμ. This filter absorbs light over the range at which the photodynamic effect is reported to occur, and should eliminate alterations in tone due to the source of illumination employed. This has been confirmed by repeated direct observation of the calibre of arteries and arterioles, using nonfiltered and filtered light in ear chamber studies; removal of the filter causes a short initial increase in tone, followed by prolonged relaxation, despite the elimination of heating effects by retaining a heat-absorbent filter in position.

ADMINISTRATION OF DRUGS

Gaseous agents were administered by Gaddum's apparatus in which the rabbit's nose and mouth are inserted through a hole in an elastic membrane into a container.

Fresh gas is introduced and used gas is removed by separate tubes, entering the container. Each tube has a low resistance one-way valve.

Irritant gases produce breath-holding by the rabbit which results in hypercarbia. This was avoided as far as possible by a slow induction when using ether, chloroform and trichlorethylene.

In order to obtain a fairly complete saturation of the animal with the agent, anaesthesia was continued for $\frac{1}{2}$ to $\frac{3}{4}$ hour before observations of the vessels were recorded. During this interval any effects from breath-holding would have disappeared.

The depth of anaesthesia with inhalation agents was gauged by the type of respiration, intercostal paresis occurring in deeper planes. The rapidity of response of the corneal reflex was useful in determining the lighter planes, and voluntary movements when the rabbit's nose

was touched were employed to indicate the return of consciousness.

Gases were delivered by a standard anaesthetic apparatus. Volumes were measured by recently calibrated rotameters. Volatile agents were vapourized by an air current passing through a Boyle's bottle. A minimum flow of 2 litres per minute was maintained throughout to prevent accumulation of CO_2.

The marginal vein of the ear was employed for intravenous injections. The depth of anaesthesia with thiopentone was determined by the corneal reflex which persists until deep levels of hypnosis are obtained.

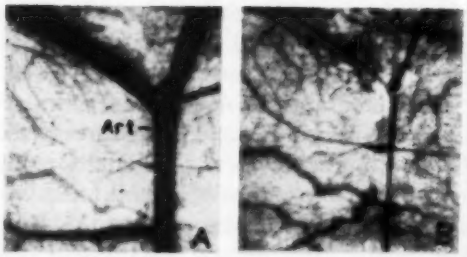

FIG. 1
(a) Control (Art.=artery).
(b) After 1:1 pitressin 0.5 ml (note dilatation of small vessels accompanying arterial constriction).

EXPERIMENTS AND RESULTS

(1) In order to assess the intensity of arterial constriction in a preliminary experiment an injection of 0.5 ml of 1:1 pitressin, that is 5 pressor units, was given. The artery emptied almost completely (fig. 1b) and the small vessels dilated as would be anticipated from the closed-space hypothesis (vide infra). The chamber which illustrates this experiment is the same as that illustrating the effects of N_2O, cyclopropane and ether (see figs. 2, 3, 4).

A. Effects of Anaesthetics

(2) *Nitrous Oxide.*

Nitrous oxide was given in 80 per cent concentration with oxygen but this was insufficient to anaesthetize the rabbit. The concentration was then raised to 95 per cent until voluntary movement had stopped, when it was reduced to 90 per cent.

During induction with 80 per cent N_2O and 20 per cent O_2 (fig. 2b) slight arteriolar dilation was observed, due probably to

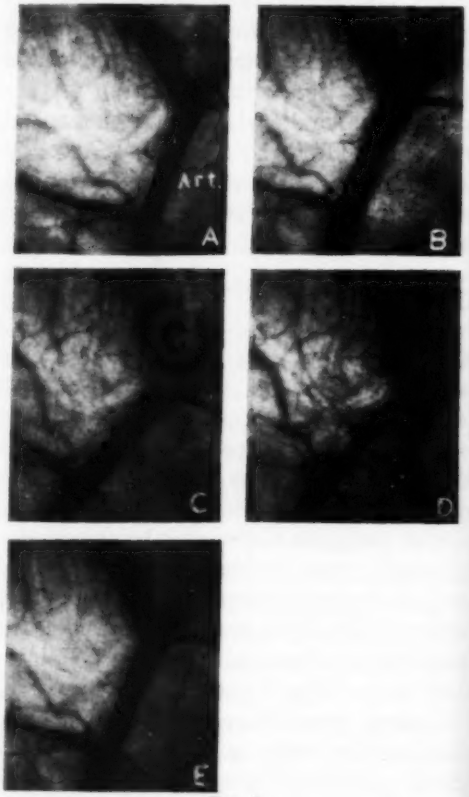

FIG. 2
(a) Control (Art.=artery).
(b) N_2O 80% and O_2 20%.
(c) N_2O 95% and O_2 5%: arterial dilatation.
(d) N_2O 90% O_2 10%: arterial constriction.
(e) N_2O 90% and O_2 10%: four minutes later (compare control).

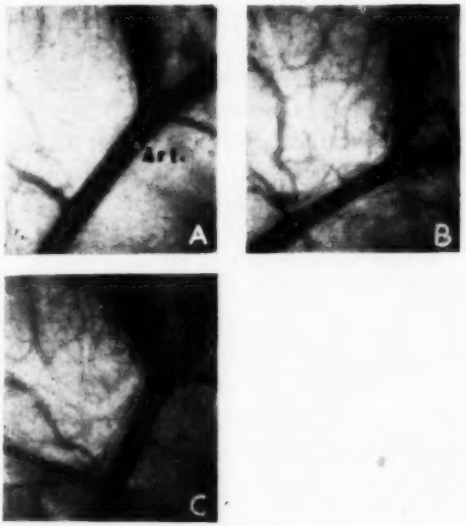

FIG. 3
(a) Control (Art.=artery).
(b) Cyclopropane 50%, O_2 50%: arterial constriction.
(c) Air: 10 minutes later: persistent arterial constriction.

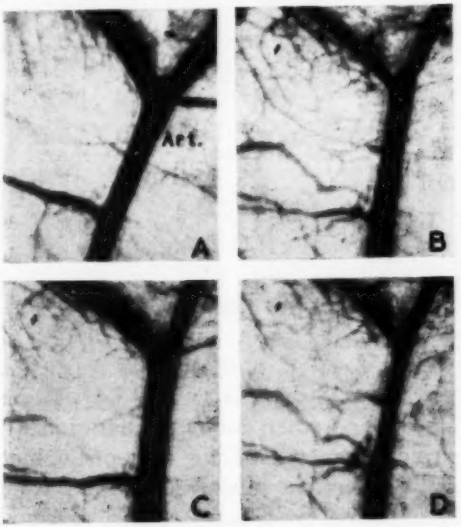

FIG. 4
(a) Control (Art.=artery).
(b) Ether: light anaesthesia: arterial constriction.
(c) Ether: deep anaesthesia: arterial dilatation.
(d) Rabbit conscious: arterial constriction.

breath-holding with CO_2 accumulation. With high concentration the vasodilatation (fig. 2c) is presumably due to the anoxia (5 per cent O_2), for the vessel became constricted (fig. 2d) when 10 per cent O_2 was given. It can be noticed in this figure that small vessel dilatation accompanies arterial constriction in accordance with the rigid space hypothesis concerning ear chambers.

Four minutes later while breathing 10 per cent O_2 and 90 per cent N_2O the vessels returned to normal (compare figs. 1e and 1a). It is concluded that N_2O had no direct effect on the artery studied, in contradiction to the findings of Seldon et al. (1942) who reported vasoconstriction in arteries and capillaries. All changes observed could be explained by changes in the tension of O_2 and CO_2 in the circulating blood.

(3) *Cyclopropane.*

Cyclopropane was given in 50 per cent concentration with O_2 when arterial constriction was observed (fig. 3b) which persisted for more than ten minutes after the rabbit started breathing air again (fig. 3c). Vasodilatation of the small vessels once again accompanied constriction of the artery. Increased vasomotion was noticed.

These results agree with those of Seldon et al. (1942) although their interpretation of the mechanism of this capillary dilatation in a closed chamber is open to doubt.

(4) *Ether.*

Ether vapour was given. In light anaesthesia when the corneal reflex first disappeared arterial constriction occurred (fig. 4b). With increasing depth arterial dilatation was seen (fig. 4c), and finally,

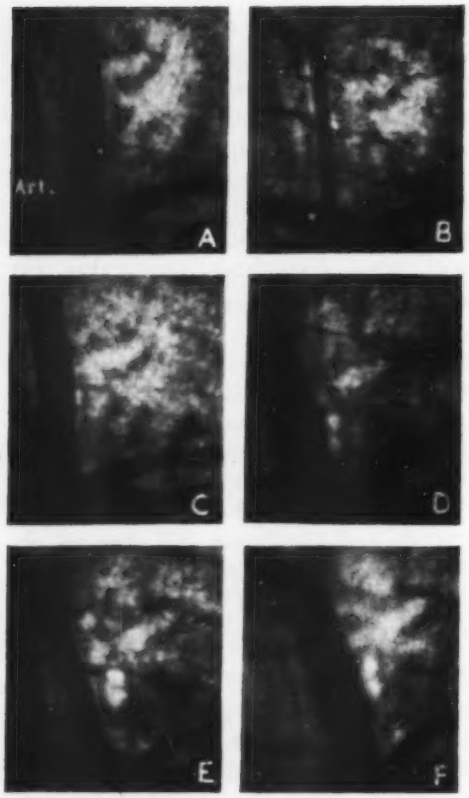

FIG. 5
(a) Control (Art.=artery).
(b) Atropine 0.2 mg: arterial constriction 15 seconds later.
(c) Three minutes after atropine: artery normal.
(d) Ether: deep anaesthesia: arterial dilatation.
(e) Ether: light anaesthesia: arterial constriction.
(f) Ether: deep anaesthesia: arterial dilatation.

with return of consciousness, arterial constriction re-appeared (fig 4d).

(5) *Ether and Atropine.*

During the previous experiment a copious oral and bronchial secretion occurred, and it was decided to repeat it with a preliminary intravenous injection of atropine 0.2 mg, which produced a profound arterial constriction in fifteen seconds (fig. 5b), returning to normal in three minutes (fig. 5c). Ether was then given and arterial dilatation occurred when a deep plane was reached (fig. 5d). When anaesthesia was lightened, arterial constriction occurred (fig. 5e), and when it was deepened again arterial dilatation (fig. 5f) recurred.

When the animal was allowed to awake constriction occurred, followed by dilatation and finally a return to normal.

Seldon et al. (1942) reported only an arterial constriction which may have been due to a lighter plane of anaesthesia during the experiment.

(6) *Chloroform.*

Chloroform was given to a rabbit whose ear chamber included the central ear artery (fig. 6a). Progressive arterial constriction (figs. 6b, 6c) occurred during induction and compensatory dilatation of small vessels in accordance with the closed-space hypothesis is clearly seen, and vasomotion was marked (figs. 6d, 6e). With increasing depth vasodilatation recurred (fig. 6f) but was not comparable with the original state of tone (fig. 6a).

The animal was now allowed to recover when arterial constriction reappeared (fig. 6g). With the return of the corneal reflex arterial dilatation again appears (fig. 6h), being interrupted by a short period of anoxia due to an obstructed airway. The anoxia was accompanied by constriction (fig. 6j) and when relieved dilatation recurred and increased (fig. 6k) until voluntary movements occurred. These were accompanied by arterial constriction and vasomotion (figs. 6l, 6m).

It will be noted that the calibre of small vessels (capillaries and venules) bears an

inverse relationship to the size of the arteries. This once again illustrates the passive behaviour of these non-contractile vessels in a rigid space and emphasizes the fact that observations on ear chambers allow no conclusions to be drawn as to the effect of a pharmacodynamic agent on these minute vessels.

(7) *Trichlorethylene.*

Administration of trichlorethylene in air produced slight constriction in the arteries accompanied by dilatation of the veins and small vessels (fig. 7b). On withdrawing the anaesthetic arterial dilatation occurred (fig. 7c), and on awakening this was reversed and profound constriction

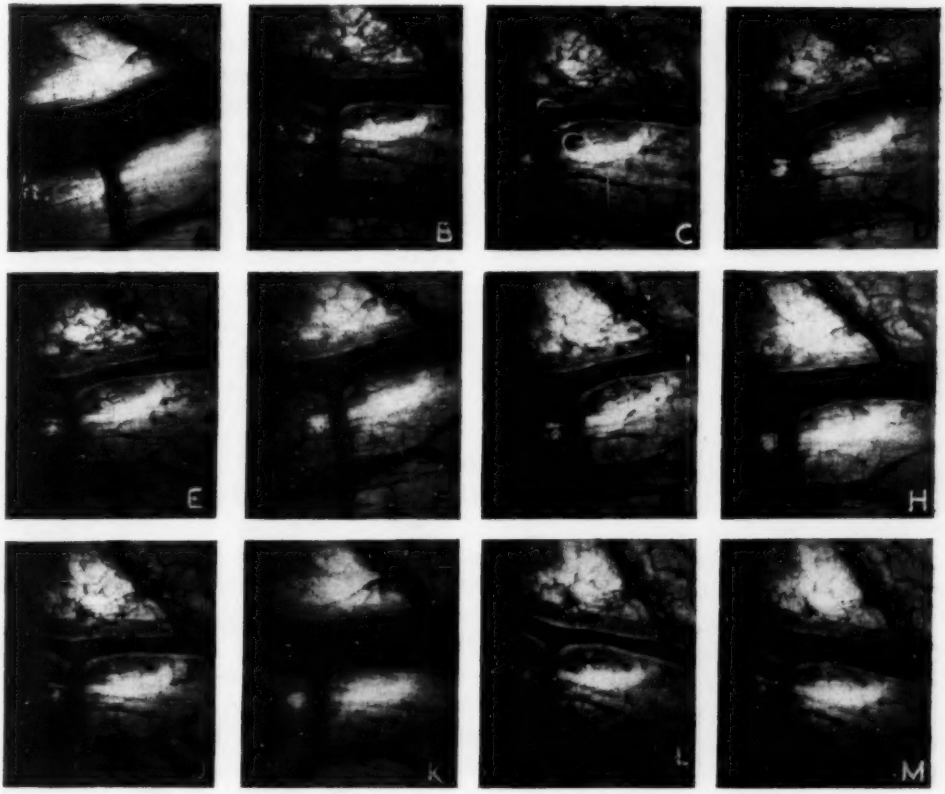

FIG. 6

(a) Control: note large central ear artery (Art. = artery).
(b) Chloroform: very light anaesthesia: arterial constriction (note compensatory dilatation of small vessels).
(c) Chloroform: light anaesthesia: progressive arterial constriction.
(d, e) Chloroform: light anaesthesia: two phases of vasomotion.
(f) Chloroform: deep anaesthesia: arterial dilatation (note disappearance of small vessels).
(g) Chloroform: light anaesthesia: arterial constriction.
(h) Rabbit conscious: arterial dilatation.
(j) Conscious, anoxia: arterial constriction.
(k) Conscious oxygenated: arterial dilatation.
(l, m) Conscious: two phases of vasomotion.

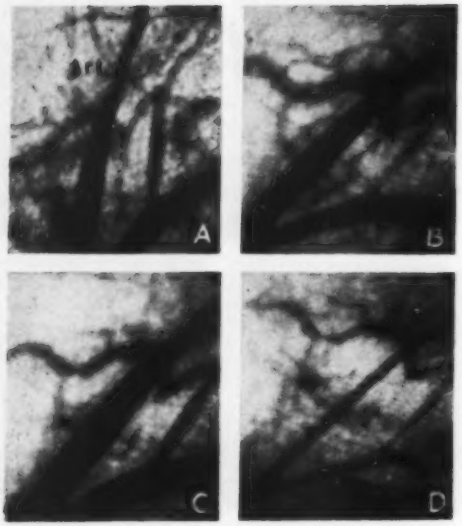

FIG. 7

(a) Control (Art.=artery).
(b) Trichlorethylene: light anaesthesia: arterial constriction (compare artery in lower right field).
(c) Air: still anaesthetized: arterial dilatation.
(d) Rabbit conscious: arterial constriction.

(fig. 7d) accompanied the reappearance of voluntary movements.

(8) *Thiopentone.*

Thiopentone was injected intravenously in 0.5 per cent solution in divided doses of 5 mg/kg to avoid the fall in blood pressure which follows the rapid injection of an anaesthetic dose. After 20 mg/kg had been given the arteries were slightly dilated (fig. 8b). ββ methyl ethyl glutarimide (Megimide) was then given in 0.5 solution in a dose of 10 mg/kg. This produced a moderate arterial constriction and compensatory dilatation of the small vessels (fig. 8c).

Further administration of thiopentone in 5 mg/kg increments up to 15 mg/kg (making the total dose 35 mg/kg) reversed the arterial constriction and restored the picture to normal (figs. 8d, 8a).

Seldon et al. (1942) reported dilatation of both arteries and smaller vessels. We have found that, whilst arterial tone is decreased, the small noncontractile vessels in a rigid chamber do not dilate, but, on the contrary, passively collapse.

B. Effects of Relaxant Agents

It was decided to investigate the effects of relaxant drugs on the preparation. For this purpose paralysing doses were injected intravenously and artificial respiration by intermittent positive pressure employed, using a pump delivering 100 mg per stroke at a rate of 18 cycles per minute until voluntary respiration returned.

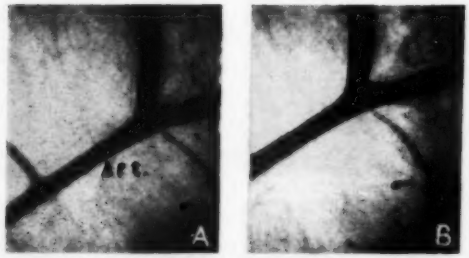

FIG. 8

(a) Control (Art.=artery).
(b) Thiopentone 20 mg/kg: arterial dilatation.
(c) Megimide 10 mg/kg: arterial constriction.
(d) Thiopentone 15 mg/kg: arteries normal.

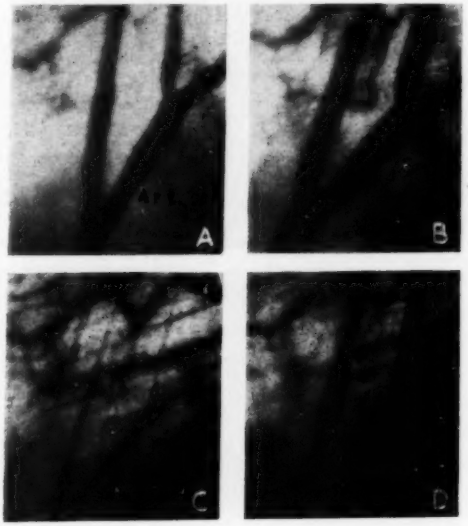

FIG. 9
(a) Control (Art.=artery).
(b) d-Tubocurarine 0.6 mg/kg: slight arterial dilatation.
(c) Normal respiration: arterial constriction.
(d) Two minutes later: normal arterial tone.

(9) *d-Tubocurarine Chloride.*

d-Tubocurarine (0.06 mg/kg) was given and a slight arterial dilatation occurred (fig. 9b).

When artificial respiration was discontinued and voluntary respirations were resumed a profound arterial constriction occurred (fig. 9c). This was presumably due to the rabbit becoming active (cf. vasoconstriction with recovery from anaesthesia (figs. 4d, 7d)) and the vessel again approached normal tone in two minutes (fig. 9d).

(10) *Gallamine Triethiodide* (*Flaxedil*).

0.15 mg/kg of gallamine triethiodide was given. This was followed in one minute by a slight transient arterial constriction (fig. 10b) which was relieved after a further minute, there being a slight dilata-

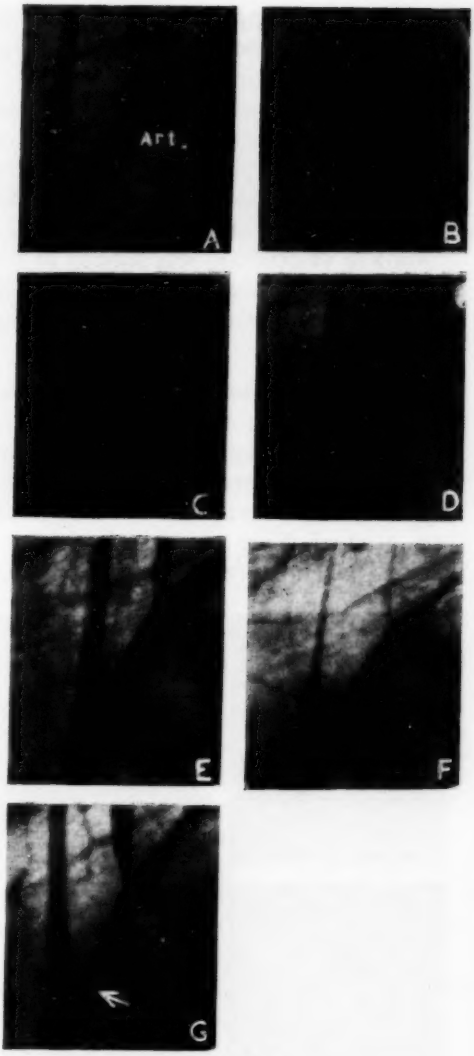

FIG. 10
(a) Control (Art.=artery).
(b) Gallamine thiethiodide 0.75 mg/kg: arterial constriction.
(c) One minute later: arterial dilatation.
(d) Paralysed: application of painful stimulus: arterial constriction.
(e) Normal respiration: arterial tone normal.
(f) Normal respiration: painful stimulus: increased arterial constriction.
(g) Vasomotion: the arrow indicates a wave of contraction passing along the artery.

tion (fig. 10c). Application of a painful stimulus at this time by squeezing the ear produced constriction (fig. 10d).

Resumption of voluntary breathing had no effect on the artery (fig. 10c), but a painful stimulus now produced a more profound constriction than that during the period of paralysis (fig. 10f).

Marked vasomotion was noticed at the completion of the experiment and fig. 10g shows a wave of contraction passing along the artery.

(11) *Suxamethonium Chloride (Scoline)*

Suxamethonium chloride was given in a dose of 0.5 mg/kg. A profound arterial constriction followed two minutes later (fig. 11b) and subsequent dilatation was very gradual. Nine minutes after the injection, when normal respiration was established (fig. 11c), a residual moderate constriction was present.

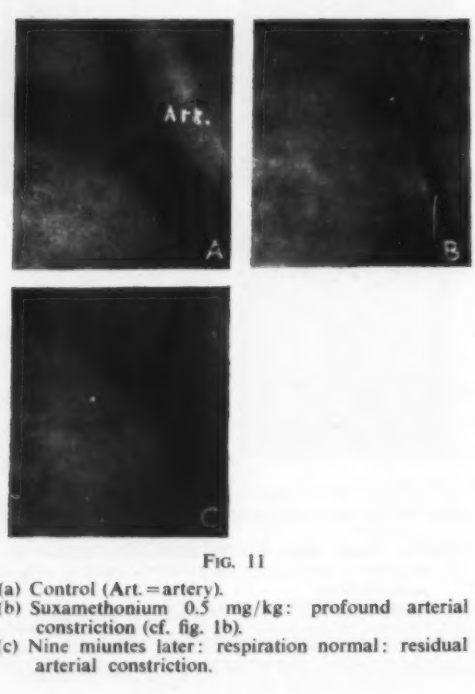

FIG. 11

(a) Control (Art. = artery).
(b) Suxamethonium 0.5 mg/kg: profound arterial constriction (cf. fig. 1b).
(c) Nine miuntes later: respiration normal: residual arterial constriction.

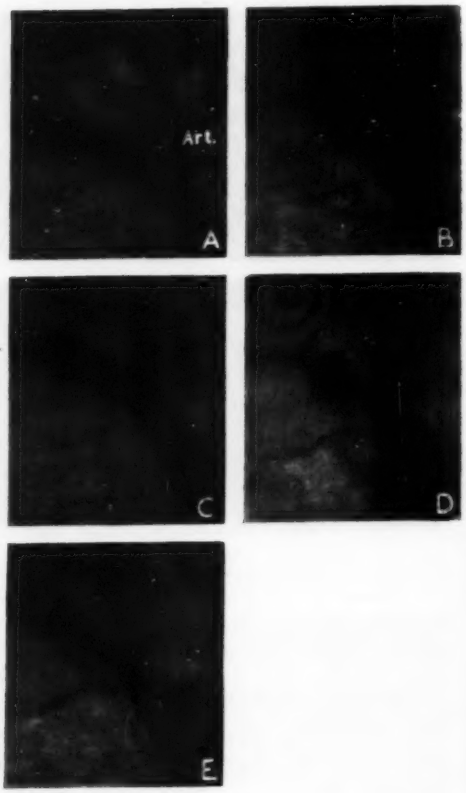

FIG. 12

(a) Control (Art. = artery).
(b) Thiopentone 20 mg/kg: slight arterial constriction.
(c) Suxamethonium 0.5 mg/kg: temporary apnoea: arterial dilatation.
(d) One minute later: arterial tone similar to fig. 12b.
(e) Conscious: arterial dilatation.

(12) *Thiopentone and Suxamethonium.*

As it was thought that the constriction produced by suxamethonium may have been due to conscious influences, 20 mg/kg of thiopentone was given. This produced slight arterial constriction (fig. 12b) which was probably due to the fall in

blood pressure which follows the rapid administration of this agent. Suxamethonium 0.5 mg/kg was then given. A marked dilatation followed (fig. 12c) before artificial respiration was commenced, but one minute after the injection the vessel had returned to the same state (fig. 12d) as that following the thiopentone (fig. 12b).

With the return of consciousness a slight dilatation occurred (fig. 12e) but tone was still greater than in the control observation.

(13) *Nerve Block of Ear and Suxamethonium.*

In order to find whether suxamethonium had any direct effect on the artery, the nerves at the base of the ear were blocked by infiltration with 0.1 per cent lignocaine solution. Figure 13a shows relaxation of tone following the ear block.

Injection of suxamethonium 0.5 mg/kg then produced a profound constriction (fig. 13b) similar to that following its administration in the conscious rabbit (fig. 11b). Progressive dilatation followed until four minutes later (fig. 12c) the vessel reached its former state of dilatation.

(14) *Hexamethonium.*

2 mg hexamethonium/kg were given and a mild arterial dilatation followed (fig. 14b). A painful stimulus was applied and minimal constriction followed (fig. 14c) instead of the usual marked arterial change. One minute after the painful stimulus the artery was still dilated (fig. 14d).

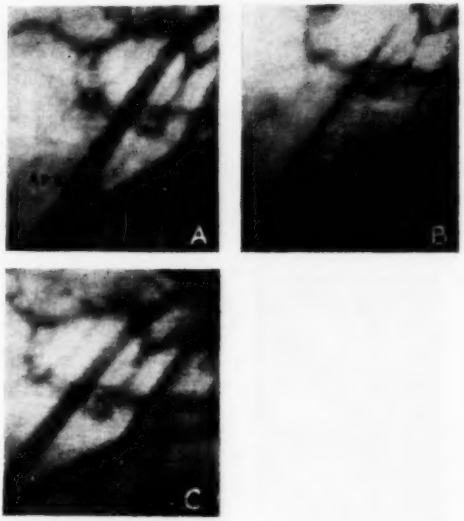

FIG. 13
(a) Nerves to ear blocked: arterial dilatation (Art.=artery).
(b) Suxamethonium 0.5 mg/kg: profound arterial constriction (cf. fig. 11b).
(c) Four minutes later: arterial tone as in (a).

DISCUSSION AND CONCLUSION

Ear chambers provide an ideal method for the direct visual observation of the effects of drugs on *arteries and arterioles*. It is clear, however, that changes in calibre of *capillaries and noncontractile vessels*, observed in these chambers, do not present a true picture of dynamic changes taking place in tissues which can increase or decrease in total volume. For this reason no legitimate conclusions can be drawn from calibre changes in capillaries and small noncontractile vessels, observed in an ear chamber during anaesthesia. It follows, moreover, that it is not legitimate to use evidence from ear chamber studies (Seldon et al., 1942) to support the suggested relationship between capillary dilatation and bleeding during surgical procedures with certain anaesthetics. The reciprocal relationship between contractile and noncontractile vessels in a rigid ear chamber is clearly demonstrated by the action of

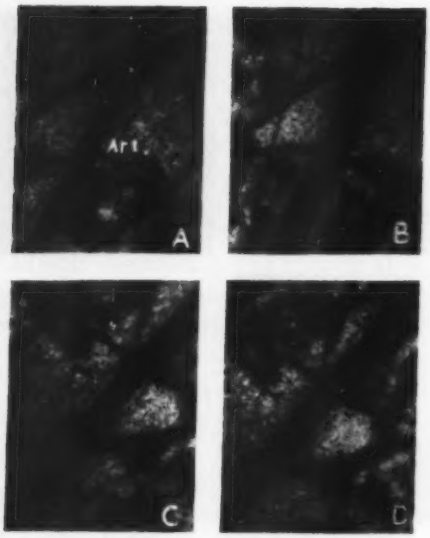

FIG. 14
(a) Control (Art.=artery).
(b) Hexamethonium 2 mg/kg. arterial dilatation.
(c) Painful stimulus: minimal constriction.
(d) One minute later: minimal change in arterial tone.

pitressin (figs. 1a, 1b), N_2O (figs. 2a, 2d), cyclopropane (figs. 3a, 3b), ether (figs. 4a, 4d), chloroform (figs. 6a to 6m) and other agents.

However, ear chamber techniques provide a clear demonstration of changes in the tone of *contractile vessels*, although any interpretation must take into account the variations in the normal tone, particularly those brought about by phasic physiological variation, that is, "vasomotion".

During anaesthesia, it has been shown repeatedly that hypoxia and hypercarbia, inadvertently produced, cause a marked variation in vascular tone. This factor must be kept in mind constantly in assessing the intrinsic effect of anaesthetics and other agents on vascular tone.

Also, changes in the systemic arterial pressure tend to produce variations in vascular tone. A fall in blood pressure to shock levels is invariably associated with marked vasoconstriction. Minor variations in arterial pressure are associated with variations in vascular tone, although it is difficult to determine which change is primary. Folkow (1949, 1952), from studies on reactive hyperaemia following temporary arterial occlusion in a limb, postulates that a fall in intravascular pressure, by reducing the stretching stimulus to the vascular smooth muscle, results in a decrease in tone—a conclusion supported by Hilton (1953), Patterson and Shepherd (1954) and Greenfield and Patterson (1954). The effect of this factor in our experiments is not known. Whilst the blood pressure can be readily recorded in the ear of the rabbit (Grant and Rothschild, 1934; Anderson, 1922) the pressure recorded at different sites on the central artery varies greatly with the size of the vessel proximately and a method of measuring the pressure in the length of vessel under observation in the chamber has not been developed.

For the inhalation anaesthetic agents tested, except N_2O, a light plane of anaesthesia invariably produced arterial constriction. This supports the current view that anaesthetics initially stimulate the vasomotor centre. In the case of ether and chloroform, a deep plane of anaesthesia was produced, and arterial dilatation ensued, presumably due to depression of the vasomotor centre. These changes are reversible by altering the plane of anaesthesia.

In the case of nitrous oxide anaesthesia, all changes in the vascular calibre ob-

served can be explained in terms of changes in oxygenation and CO_2 retention. In our opinion the difficulty encountered in inducing a steady plane of anaesthesia with this anaesthetic agent in an unpremedicated rabbit, without hypoxia, invalidates any evidence that nitrous oxide has a direct pharmacological action on vascular smooth muscle.

Arterial constriction produced by cyclopropane (fig. 3b), as reported by Seldon et al. (1942), agrees with present clinical impressions that cyclopropane anaesthesia, without CO_2 retention, is not accompanied by increased arteriolar bleeding.

Return of consciousness and voluntary movements, following anaesthesia were invariably accompanied by a marked increase in vascular tone—always in excess of the initial tone prior to anaesthesia (see figs. 4d, 6l).

Thiopentone produced a diminished vascular tone, as reported by Seldon et al. (1942). It was found that ββ ethyl methyl glutarimide (Megimide), which has been reported as a barbiturate antagonist by Shaw et al. (1954), produced arterial constriction, reversed by additional doses of thiopentone (figs. 8c, 8d).

The investigation of relaxant drugs on vascular tone in the conscious animal presents great difficulties. These agents necessitate the use of artificial respiration, which has a complicating effect on vascular tone by causing nervous stress; and in the case of intermittent positive pressure respiration, as used, venous return is said to be impaired (Cournand et al., 1948). The results obtained suggest that d-tubocurarine which produces a diminution in vascular tone, depresses preganglionic sympathetic synapses without preliminary stimulation. This depression is not complete with a dose employed to produce respiratory paralysis, in that a subsequent painful stimulus produced intense constriction.

Gallamine triethiodide appeared to produce a preliminary stimulation before depression (figs. 10b, 10c). Again, block was incomplete as pain produced constriction (fig. 10d) but not comparable to that produced by a similar pain stimulus after paralysis had worn off (fig. 10f). Suxamethonium produced profound constriction in an artificially respired conscious animal (fig. 11b). When the drug was preceded by a hypnotic dose of thiopentone, and after respiration was artificially stabilized, the constriction was still present (fig. 11d). It is considered that this constriction produced by suxamethonium is not an artifact due to respiratory embarrassment or nervous excitation, suggesting there is either a direct effect on vascular smooth muscle or sympathetic ganglionic stimulation. The central effect was abolished by blocking the vasomotor nerves at the base of the ear, with consequent reduction in tone (fig. 13a). Suxamethonium still produced profound vascular constriction (fig. 13b) followed by gradual return to the initial dilated state (fig. 13c). This suggests that suxamethonium directly stimulates vascular smooth muscle.

Arterial dilation followed the exhibition of hexamethonium (fig. 14b) in accordance with its ganglion blocking properties (Paton and Zaimis, 1949). A subsequent painful stimulus produced a minimal change in calibre (fig. 14c) indicating a block, more complete than that apparently produced by curare and gallamine.

SUMMARY

(1) The effects of anaesthetics, relaxant agents and hexamethonium, on vascular smooth muscle have been studied by the preformed tissue Sandison Clark ear chamber technique in the rabbit.

(2) The limitations and interpretations of the behaviour of contractile and non-contractile vessels, in ear chambers, are discussed.

(3) The results obtained have been described, and interpreted with due attention to complicating factors such as oxygen lack, CO_2 excess, nervous stress and variations in systemic blood pressure.

ACKNOWLEDGMENTS

We are grateful to Professor David Slome for his interest in this work, and to the H.N. Smith Research Unit, Royal College of Surgeons of England, for granting facilities; to Nicholas Laboratories Pty. Ltd., Slough, for supplies of Megimide; and to A. Charles King Ltd. for the loan of anaesthetic equipment.

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EDITORIAL—*continued*

In his judgment, the Presiding Judge, Mr. G. Glynn Blackledge, Q.C., said that he was satisfied that the extravenous injection of a small quantity of solution could happen without any negligence on the part of the operator. He held that Dr. I.P.C. had followed the correct technique and had stopped the injection as soon as he realized that the point of the needle was outside the vein. He found no evidence of negligence on the part of Dr. I. P. C. and accordingly gave judgment for the defendants with costs.

The importance of this judgment, with its implication, that " res ipsa loquitur " is not always proof of negligence, cannot be overemphasized.

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A COMPARISON OF THE ANTISIALOGOGUE ACTION OF ATROPINE AND HYOSCYAMINE

BY

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SINCE its introduction fifty years ago as a means of depressing salivary activity before the administration of an anaesthetic, atropine has become probably the most commonly used drug for this purpose. It is without question an extremely useful antisialogogue, but has nevertheless some disadvantages—the tachycardia produced by it is sometimes undesirable, and every anaesthetist will recall cases which have been "wet and bubbly" in spite of it. In a recent paper, Mushin et al. (1953) showed that atropine sulphate 1/100 grain (0.65 mg), the usual pre-operative dose, depresses salivary activity by only 50 per cent, so that it is by no means ideal for this purpose.

In 1953 Griggs and Berson reported a study of "drying" agents in paediatric premedication. Among the drugs evaluated was hyoscyamine (Bellafoline), which is the levo isomer of the alkaloid tropine tropate; atropine is the racemic product of an equimixture of d- and l-tropine tropate, and does not occur at all in the natural belladonna plant, but is formed only during the process of isolation. In this and a subsequent paper (Griggs and Adriani, 1954) the authors found atropine unsatisfactory as a drying agent as compared with hyoscyamine; however, the observations were purely clinical and they do not state what their criteria were for a satisfactory drying effect. Because of their claim that hyoscyamine produced satisfactory drying in 90 per cent of cases, as compared with only 69 per cent with atropine, it seemed that a more objective method of comparing the two drugs might help to throw more light on the matter.

METHOD

The method used was that described by Mushin et al., and is briefly as follows. After clearing the mouth of saliva, 0.3 ml of lemon juice is placed on the tongue and allowed to act for 30 seconds; the mouth is then rinsed for 15 seconds with 5 ml of water, and for a further 15 seconds the mouth is emptied by repeatedly spitting into a measuring cylinder. After settling the froth with caprylic alcohol, the reading taken, minus 5 ml, is the salivary secretion in response to a constant, almost maximal stimulus.

This amount, known as the salivary index, was measured at intervals until 5 "normal" values had been obtained. The drug to be tested was then injected subcutaneously over the deltoid muscle in the arm, and the index was measured and the pulse counted at 10-minute intervals until the index had returned to normal, or nearly so. Altogether nine volunteers were

tested, and a series of paired results obtained. Each subject was given atropine sulphate on one day and hyoscyamine (Bellafoline) on another day, the dosage in each case being 1/100 grain (0.65 mg).

RESULTS

Subjective sensations. All the subjects felt dry at the height of action of the drugs, two of them not as dry after hyoscyamine as after atropine. Whilst none complained of dizziness after atropine, five of the nine did so after hyoscyamine, two of them quite severely so. One had a transient choking feeling, and another a marked but also transient shortness of breath after the hyoscyamine. There was also a very marked drowsiness in three of the subjects, who seemed to have great difficulty in keeping awake in the intervals between the measurements. The atropine did not seem to produce drowsiness in any of the subjects. Two of the subjects complained of blurring of vision and difficulty in reading at the height of action of the atropine.

An interesting point worth recording is that every one of the nine subjects complained during the administration of the hyoscyamine of severe stinging at the site of injection, whereas the atropine was relatively painless.

The pulse rate. The mean pre-injection rate for each subject was taken as 100 per cent and the postinjection values expressed as a percentage. Figure 1 is a graph of the mean values of these percentages for all the subjects, and shows the expected initial slowing of the rate after atropine; with the hyoscyamine, however, this slowing was less noticeable, and really only occurred in two of the subjects. The subsequent tachycardia was more marked following hyoscyamine (in one subject it was as high as 167 per cent of normal, and in another

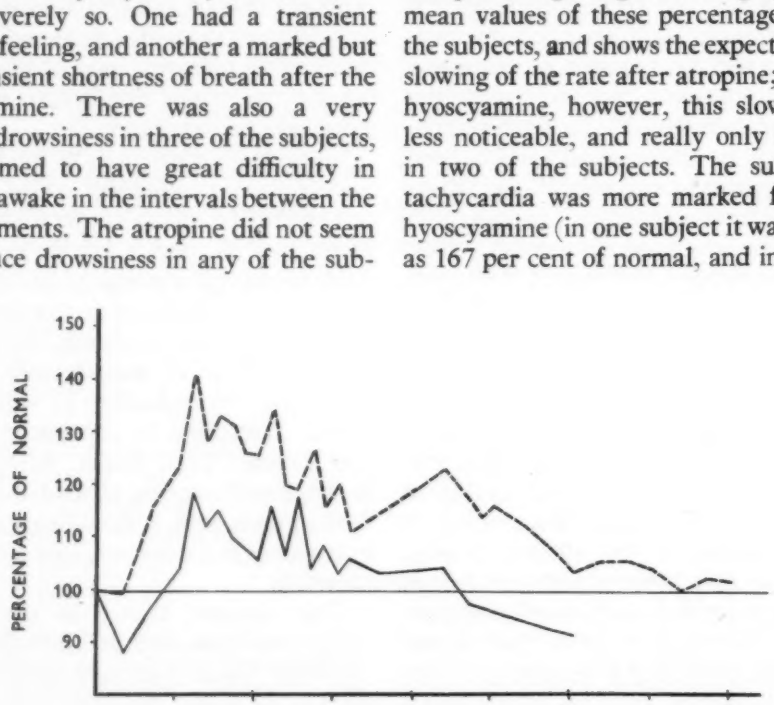

FIG. 1
Pulse Rate, Mean Percentages of Normal
———— Atropine sulphate.
— — — — Hyoscyamine.

159 per cent), and it also appeared to be maintained above normal for a longer period than after atropine.

In one subject, hyoscyamine produced a marked irregularity of the pulse rhythm; this consisted of numerous extrasystoles which appeared at the time of his maximum depression of salivary activity (1 hour after the injection), and persisted for 50 minutes thereafter.

Saliva. Table I shows the average of the pre-injection values for each of the subjects on the two separate days of the experiment. It can be seen that, whilst there is a considerable difference between the levels for different subjects, there is no significant difference between the two readings for each subject. This is taken as a strong confirmation that the method is an extremely reliable one for estimating salivary activity.

TABLE I

Difference between the means of the pre-injection saliva values

Subject	Before Atropine	Before Hyoscyamine	Difference (A−H)
D.K.V.	4.86	6.06	−1.20
M.B.	4.36	4.26	+0.10
L.P.N.	6.78	7.00	−0.22
P.L.P.	5.48	5.36	+0.12
S.P.S.	7.87	7.66	+0.21
C.N.M.K.	6.61	5.36	+1.25
D.C.	5.94	6.60	−0.66
P.M.	7.24	6.30	+0.94
C.M.	6.38	7.50	−1.12
—	—	—	−0.58

Mean of the differences = −0.0644;
t = 0.0212, therefore not significant.

Figure 2 shows a composite graph of all the postinjection salivary values, expressed in percentage form, the average pre-injection level for each subject being taken as 100 per cent. From this it appears that with both drugs the maximal salivary depression occurs between ½–1 hour after injection, also that with atropine the maximum depression is 72 per cent of normal, whilst with hyoscyamine it is 78 per cent. It should be noted here that, between the period of ½ and 1½ hours after injection, the index was measured at 5-minute intervals, following the recommendation of Mushin et al., in order to determine more accurately the time of maximum depression.

Consider table II, however. This shows that in only two subjects (S.P.S. and C.N.

TABLE II

Minimum salivary indices (percentage of normal) and the earliest intervals after injection at which they were attained.

Subject	Minimum salivary level (% of normal)			Earliest time at which minimum level was attained		
	Atropine	Hyoscyamine	Difference (A−H)	Atropine Min	Hyoscyamine Min	Difference (A−H)
D.K.V.	20.7	23.1	− 2.4	20	45	−25
M.B.	32.0	21.1	+10.9	30	75	−45
L.P.N.	32.4	21.1	+11.0	40	40	0
P.L.P.	36.5	24.2	+12.3	30	35	− 5
S.P.S.	36.8	30.1	+ 6.7	50	40	+10
C.N.M.K.	13.6	11.2	+ 2.4	40	20	+20
D.C.	13.4	22.7	− 9.3	35	75	−40
P.M.	27.6	15.9	+11.7	50	50	0
C.M.	42.3	33.3	+ 9.0	30	50	−20
Mean	28.3	22.5	+ 5.81	36	48	−11.6
t			2.33			1.46
Significance			At 5% level			None

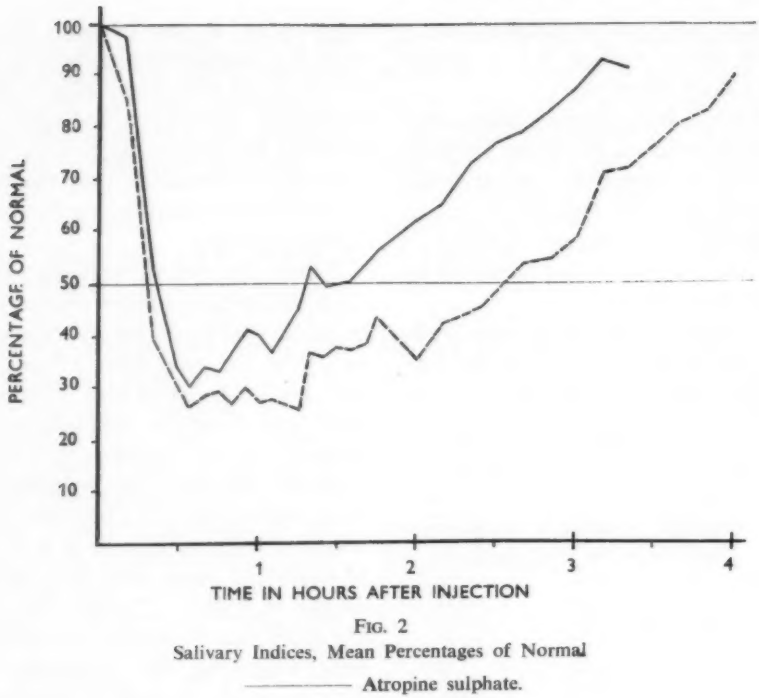

FIG. 2
Salivary Indices, Mean Percentages of Normal
———— Atropine sulphate.
— — — — Hyoscyamine.

M.K.) was the maximum depression attained earlier with hyoscyamine than with atropine, the average time being 48 minutes with hyoscyamine and 36 minutes with atropine. It can also be seen that in all but two subjects, the maximum depression was greater for hyoscyamine than for atropine. Statistical analysis of these levels reveals that the difference is significant, in other words, it appears that, dose for dose, the maximum drying effect is greater with hyoscyamine than with atropine.

Further consideration of figure 2 appears to show that with hyoscyamine a longer time is taken to return to normal than with atropine, and table III confirms that this is the case. This delayed return to normal with hyoscyamine was a completely unexpected finding, and because no allowance had been made for it, the readings had to be discontinued after 4 hours, even though the values had not returned altogether to their pre-injection levels.

DISCUSSION AND CONCLUSIONS

From the results it is clear that, at its maximum peak of action, the drying of saliva produced by hyoscyamine is greater than that following the same dose of atropine, the maximum effect is maintained rather longer, and the return to normal is more delayed. It is interesting to note here that the maximum level of depression following atropine (by 72 per cent of

TABLE III
Salivary indices, mean levels and differences at various intervals of time (percentage of normal)

Time after injection	Atropine	Hyoscyamine	Mean Difference (A—H)	*t*
1 hr	40.6	28.7	+11.9	4.26*
1 hr 30 min	55.2	36.5	+18.7	5.02†
2 hr	60.3	38.9	+21.4	5.68‡
2 hr 30 min	75.5	49.4	+26.1	5.33†
3 hr	83.2	60.8	+22.4	4.44*
3 hr 30 min	—	73.8	—	—
4 hr	—	84.7	—	—

* Significant at 0.5% level. † Significant at 0.2% level. ‡ Significant at 0.1% level.

normal) is much lower than that found by Mushin et al. (56 per cent of normal).

These observations confirm the reports of Griggs et al., who found hyoscyamine to produce satisfactory drying in 89 per cent of cases, as compared to 69 per cent with atropine, basing their results on clinical impressions. The marked drowsiness following hyoscyamine in some of the subjects is in keeping with the report of Wise et al. (1954), who noticed a notable lack of apprehension in children who had received only hyoscyamine as a premedication.

Whilst none of these authors mentions any other side effects of hyoscyamine, those observed during this investigation require consideration. The severe dizziness in five of the nine subjects, and the choking feeling and shortness of breath in two, may not be of any matter in the patient lying in bed, but they may be troublesome in the ambulant patient. The marked elevation of the pulse rate in all the subjects as compared with atropine, together with the arrhythmia in one, can on many occasions be completely undesirable and, in the opinion of the author, must heavily weigh the balance against the increased drying effect provided by hyoscyamine, certainly in some, if not in all, cases where it is proposed to use it.

SUMMARY

A controlled laboratory investigation is described, comparing the salivary depressant activity of atropine with that of an equal dose of hyoscyamine (Bellafoline), using a method previously reported.

The results are discussed and analysed, and it appears that at its peak of action hyoscyamine has a greater drying effect than the same dose of atropine, the maximum effect is maintained for a longer period, and there is a slower return to normal.

The effects of both drugs on the pulse rate are compared, and various side effects are discussed.

ACKNOWLEDGMENTS

I should like to record my thanks to Professor Gillman, Professor of Physiology at the Durban Medical School, for his co-operation and help in providing facilities; to his students who so willingly volunteered for what is at best a tedious procedure; and to Professor W. W. Mushin and Dr. H. Grant-Whyte for their constant encouragement and advice.

The hyoscyamine (Bellafoline) used in this investigation was supplied by Sandoz (South Africa) Ltd.

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THE PAULING OXYGEN ANALYSER AS AN AID TO THE ANAESTHETIST

BY

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THE Pauling oxygen analyser was developed during the last war (Pauling, Wood and Sturdivant, 1946). Like one or two other commercially available instruments, it uses the principle of paramagnetism. Oxygen, alone among gases encountered in physiology and anaesthesia, is positively paramagnetic. Its molecules are attracted by a magnetic field. If an atmosphere containing oxygen is brought into a magnetic field, the oxygen molecules will at once start to migrate towards that part of the field where the flux density is greatest and congregate there, displacing other molecules.

In the Pauling analyser this principle is made use of by causing the atmosphere under test to pass slowly through the field set up by a pair of permanent magnets. The magnets are so arranged that the resultant field is symmetrical and contains two zones of maximum flux density. In the field are suspended two minute glass spheres, joined together by an arm to form a tiny dumb-bell, whose total weight is a few milligrammes. This dumb-bell is suspended by a fine quartz fibre in such a way that the two spheres lie close to the two points of maximum flux density. The magnetic field with its suspended dumb-bell forms the analysing chamber. Oxygen molecules admitted to it congregate at the two magnetic centres, repelling other molecules therefrom. The two spheres of the dumb-bell contain nitrogen. These nitrogen molecules are repelled, and press against the far sides of their imprisoning spheres. The two spheres, therefore, tend to move away from the magnetic centres, and a couple, or twisting action, is exerted on their suspending fibre. The magnitude of this couple is dependent on the number of oxygen molecules congregating at the magnetic centres, and hence is *proportional to the partial pressure of oxygen in the analysing chamber*. In order to measure the couple, a tiny mirror is fixed to the quartz suspending fibre. When the fibre twists, the mirror turns with it, and the beam reflected from a small lamp moves across a scale. Thus the meter measures the partial pressure of oxygen in the mixture presented to it. It is unaffected by other gases likely to be present in anaesthetic mixtures. The only power it requires is that needed for the lamp, for which a torch battery will suffice.

Through the courtesy of the Superintendent of the Admiralty Research Laboratory, Teddington, the writer was able to obtain a model "S" Pauling meter. This is light and compact (it measures 11 × 15 × 17 cm) and it can be mounted on a standard anaesthetic table. This model

was intended for analysing the air in submarines, and certain modifications have had to be made to adapt it to anaesthetic use. Its scale was originally calibrated in partial pressure of oxygen. For a submarine, in which the total pressure may vary appreciably, this is the obvious presentation, but for the gases in an anaesthetic circuit, whose pressure does not differ importantly from atmospheric (this is true even during positive pressure respiration) oxygen percentage is a more appropriate expression. Full scale deflection, in the original instrument, was given by the range 110 to 190 mm, corresponding to 14.5 per cent to 25 per cent at atmospheric pressure. For use with anaesthesia, it seemed desirable that the instrument should give information about oxygen concentrations in the range 14 per cent to 50 per cent. To adapt it to these demands, the lamp was shifted slightly, the flux density of the field was reduced by short circuiting some of the flux, and a new scale was drawn after calibration against known mixtures. The instrument contained a thermostatically controlled heater. This served three purposes: (1) it maintained the analysing chamber at constant temperature, desirable because paramagnetism varies inversely with absolute temperature: (2) it prevented condensation of moisture within the analyser; (3) the heating effect set up a convection current which caused the atmosphere in the submarine compartment to pass slowly through the analyser. In modifying the instrument the heater was disconnected. This was because it required mains electricity, it introduced a hazard of explosion, and it needed some time to warm up. The error caused by temperature changes likely to be encountered in an operating room would not be noticeable. Another means of preventing condensation had, however, to be provided. This has been done by inserting a tube of silica gel in the pathway of the gases coming to the analyser. Instead of using convection, the gases for analysis are pushed through the instrument by positive pressure, which is, of course, readily available in an anaesthetic circuit. A pressure difference of rather less than 1 cm H_2O is all that is required to pass gases at a sufficient rate through the instrument. Many expiratory valves, even when fully unscrewed, need a greater pressure than this to open, so that to allow this pressure to be developed in the system during a small part of each respiratory cycle imposes no extra burden on the spontaneously breathing patient. If pressure respiration is being used, the pressure swing in the circuit is of course far in excess of

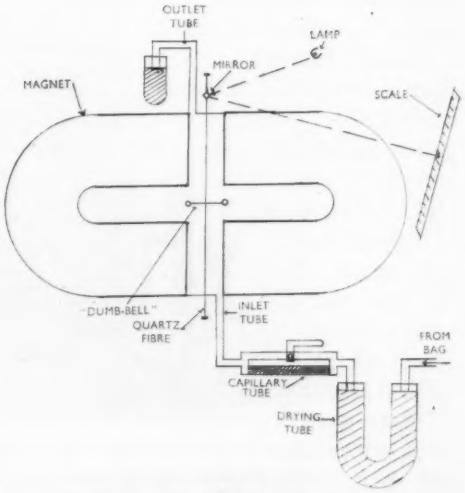

FIG. 1
Modified Pauling oxygen analyser (diagrammatic)

1 cm. A large pressure difference, if allowed to act on the analyser, would force gases through it in bursts during inspiration, and would prevent stable operation. To obviate this a short length of capillary tubing has been added. This can be interposed at will (by turning a tap) between the analyser and the anaesthetic circuit. The pressure drop in this capillary tube absorbs most of the variations imposed by pressure breathing. When it is in circuit, there is just enough pressure transmitted through it to allow gases to pass to the analyser at an acceptable rate. A visual indication of the passage of gases through the analyser was also required. This has been provided by causing them to emerge under liquid in a small tube, so that the bubbles can be seen. Water could have been used, but the liquid employed is dimethyl phthalate, which has a low vapour pressure. This completed the modifications; and the small additions—drying tube, capillary tube and bubbler tube—have been mounted on the case of the instrument. A schematic diagram of the modified analyser is shown in figure 1, and the instrument can be seen in position on a standard anaesthetic trolley in the photograph (fig. 2). It has been in routine use for nearly two years.

Gas for analysis is taken from the circuit, close to the rebreathing bag and remote from the point of entry of fresh gases. Narrow bore rubber tubing conveys it to the analyser, which is mounted on a bracket above the flowmeters and vaporizing bottles. Gas from the circuit is analysed continuously throughout anaesthesia, one or two bubbles being delivered

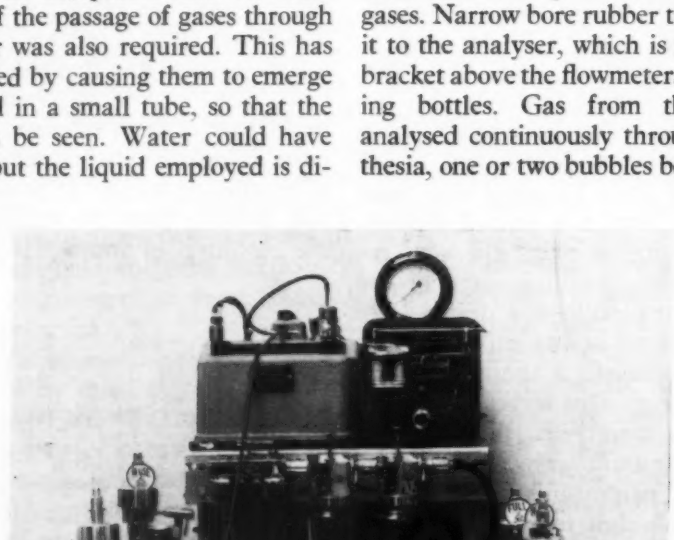

FIG. 2

The Pauling Analyser is the black box on the right, with the drying tubes and bubbler tube on the front of the case below the scale. Behind it is an anaeroid manometer to indicate intratracheal pressure. To the left of it is a Brinkman Carbovisor for continuous monitoring of CO_2 levels.

from the bubbler tube in each respiration. This represents a total flow of less than 10 ml a minute, and does not constitute a a noticeable leak. Nevertheless, the instrument reflects changes in oxygen content sufficiently rapidly for clinical use, and under these conditions indicates oxygen concentration to within about 1 per cent.

Its use allows truly closed nitrous oxide-oxygen anaesthesia. If the machine and its connections to the patient are gas-tight, a total flow of fresh gases of 400–500 ml/min is all that is used *with spontaneous breathing*. Of this flow, 250 ml may be oxygen to supply the patient's metabolic needs and make good leakage, and 150–250 ml is nitrous oxide to make good losses from leakage and from diffusion. The aim is to keep the concentration in the bag, for a healthy patient, between 22 per cent and 24 per cent. The air inspired will be of the same composition as that in the bag and connecting tubing. With this completely closed method, altering the flow of either gas by 50 ml/min will have an obvious effect on the distribution of the gases in the system. This effect is faithfully revealed by the analyser, though, of course, the indication is not immediate. It takes a few minutes for the new equilibrium to be reached throughout the system, and for a sample then to reach the analyser. It is found that after a small change in the proportion of fresh gases has been made the analyser starts to move within 2 minutes, and has settled down to its new position within 4 minutes. For the delicate control which this analyser permits, it is of course, necessary to have flowmeters for both gases which are accurate at small rates of flow, and which will indicate small changes in those rates. In the writer's machine the oxygen "rotameter" had been tested and found sufficiently accurate. For N_2O an additional rotameter covering the range 0–1,500 ml/min has been fitted. It occupies the place formerly taken by the CO_2 flowmeter. Gas is passed through the two rotameters in series, though, of course, the two readings are not summed. The "coarse" rotameter is not affected, since the "fine" rotameter, though it will *indicate* only up to 1,500 ml/min, will *pass* gas (with the float at the top of the tube) at rates up to 10 litres a minute. When a litre a minute is passing the "fine" rotameter registers 1,000 ml and the "coarse" one registers 1 litre.

With this arrangement, it is necessary only to determine the total flow of fresh gases required to keep a full bag with the expiratory valve closed, and then to find the proportion of the two gases which will yield the concentrations desired.

The correct flows can usually be arrived at within 10 minutes of the start of closed circuit anaesthesia, and thenceforward it is necessary to make only occasional alterations, of about 50 ml/min, in the flow of either gas, to maintain equilibrium. In this way, nitrous oxide—that excellent but weak anaesthetic—can be used to its fullest advantage without risk of anoxia.

It is reassuring to see the meter constantly indicating, say, 23 per cent of oxygen throughout a long closed anaesthetic, with a flow of fresh gases far lower than one would dare to use without it. The possibility of safely using nitrous oxide in such high concentrations reduces the need for non-volatile supplements, and the writer now finds that he has to use pethidine (or other supplement) very rarely.

Closed anaesthesia is preceded by a period—during and after induction—of semi-open anaesthesia with fresh gases entering the circuit at 8–10 litres a minute, and with the expiratory valve open. After 20 minutes of this the tension of nitrous oxide in the arterial blood will be about 90 per cent of that in the inspired air, and the nitrogen in the patient's body will be largely replaced by nitrous oxide (Kety, 1951). Complete replacement takes much longer than 20 minutes, but the curve relating nitrous oxide uptake to time is an exponential one, so that at the end of 20 minutes something near a steady state has been achieved, and the amounts of the two gases needed to maintain equilibrium will be approaching a minimum.*

When pressure breathing is used, because of increased leakage and diffusion, gases are lost from the system at rates of 1–1½ litres a minute: and this loss has to be made good by admitting fresh gases at a corresponding rate.

The total flow of fresh gases, in these circumstances, is that found necessary to maintain a constant mean volume in the rebreathing bag with the respiratory valve closed. The proportion of this flow which should be represented by each of the two gases can be calculated,* but the calculation requires a knowledge of the patient s oxygen consumption, and involves certain approximations, so it is not of much practical value. To be sure of avoiding anoxia, therefore, we have, in the absence of an oxygen analyser, to be over generous with the oxygen, and this generosity has to be at the expense of the nitrous oxide, which is thereby rendered less effective than it might be.

The use of the Pauling analyser obviates this difficulty. It allows the flow of fresh gases to be proportioned with considerable accuracy so as to give any desired concentration of oxygen in the inspired air, and it enables the anaesthetist to reduce this total flow to the minimum necessary to replace losses.

The writer feels that this instrument has a place in anaesthesia. With it we can combine the advantages of high concentrations of nitrous oxide with the advantages of closed anaesthesia. These latter advantages are economy, conservation of heat and moisture, accuracy of control, and the fact that volatile agents such as ether which may have been added during induction of anaesthesia, are not blown off through the expiratory valve, but may be retained in the circuit—and in the patient —if desired.

Severinghaus (1954) used a Pauling oxygen analyser to investigate the uptake of nitrous oxide by the body, and results obtained by the writer are in agreement with his. Unfortunately, these analysers are expensive and are not easily obtainable in this country.

* See Appendix.

APPENDIX

The oxygen concentration in the circuit, and hence that in the inspired air, is given by the expression:

$$O_2\% = \frac{L_{O_2} \times 100}{F_T - U_{O_2} + (D_{N_2O} - D_{N_2})}$$

where L_{O_2} = oxygen lost from the circuit by leakage
F_T = total flow of fresh gases
U_{O_2} = patient's oxygen uptake
D_{N_2O} = nitrous oxide lost from the circuit by diffusion into the patient.
D_{N_2} = nitrogen gained by the circuit by diffusion from the patient and from the atmosphere.

All in ml/min.

D_{N_2O} represents the uptake of nitrous oxide by the tissues from the arterial blood. It may be thought of as consisting of two parts. The first is that which would be taken up by the tissues if they did not lose any to the atmosphere. This uptake is a consequence of the blood/tissue gradient, and decreases exponentially with time. It is given by $\frac{1000}{\sqrt{t}}$ where t is the time in minutes from the beginning of exposure to nitrous oxide (Severinghaus, 1954). Thus after 4 minutes it would be at the rate of 500 ml/min, after 20 minutes it would be 224 ml/min, and after 100 minutes it would have fallen to 100 ml/min. The second part is that taken up, in addition, to replace nitrous oxide lost by diffusion through the intact skin and from the wound. Orcutt and Waters (1933) estimate the loss from the skin at 7 ml/min. That from the wound will depend on its extent and on the vascularity of the exposed tissues. It usually amounts to several times that lost from the intact skin. D_{N_2} can be taken as about one-thirtieth of D_{N_2O}, because nitrous oxide is about thirty times as soluble in the body as nitrogen. The term $(D_{N_2O} - D_{N_2})$ could therefore be replaced by $(0.97\ D_{N_2O})$.

The only term in the equation that is known is F_T, which is given by the flowmeters. L_{O_2} can be approximated from the total losses if it is assumed that loss by leakage of the two gases occurs in the proportion in which they exist in the circuit. U_{O_2} can be approximated from a knowledge of the patient's size and the degree to which his metabolism has been depressed by drugs. The first component of D_{N_2O} can be obtained from $\frac{1000}{\sqrt{t}}$. For its second component we may take a figure varying from 7 ml/min when there is no skin incision to one of perhaps five times the first component in such operations as thoracotomies.

It will be apparent that in most cases the approximations introduce too many inaccuracies for practical use.

ACKNOWLEDGMENT

It is a pleasure to acknowledge my indebtedness to Professor Pask who first suggested this use of an oxygen analyser to me.

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BOOK REVIEW

Hypothermic Anaesthesia. By R. W. Virtue. Published by Charles C. Thomas, Springfield, Illinois. Pp. 56. Price 18*s*.

There is no doubt that the little black books being issued by Charles C. Thomas, Springfield, are making a notable contribution to anaesthetic literature. This series, which is grouped under the general title of the "American Lectures in Anesthesiology", is edited by John Adriani, which guarantees an overall level of excellence. The example under review emanates from the Denver, Colorado, Centre, which has contributed so much to the practical application of hypothermia. In 1953 Swan, Zeavin, Blount and Virtue published a series, remarkable at that time, of 16 patients who had had surgery performed on the open heart. They had only one operative death and one post-operative fatality. This achievement was made possible by a simple method of hypothermia, which consisted of surface cooling in a bath of iced water under various forms of light anaesthesia, chiefly ether. In the prevention of ventricular fibrillation at low temperatures these workers have concentrated on over-ventilation and elimination of carbon dioxide, and the use of neostigmine. These prophylactic measures are of considerable help, but are probably not the complete answer. That they are so effective has always seemed a little surprising to the writer in view of the similarity in effect on the conducting mechanism of carbon dioxide and neostigmine.

Dr. Virtue's monograph is pleasing in many ways; not least perhaps, because he underrates if anything the notable contributions of his own unit, and also shows himself to be well acquainted with the work which has been done in centres outside the United States.

The eleven chapters are an extremely helpful summary of the literature up to the end of 1954. They are clearly and simply written, printed in pleasant type on good paper, and a quick reading revealed only one minor typographical error. What more could one ask of a monograph of 56 pages?

T. Cecil Gray

Brit. J. Anaesth. (1956), **28**, 124

THE USE OF AIR IN HIBERNATION ANAESTHESIA

BY

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HIBERNATION anaesthesia as described by Smith and Fairer (1953), has been used in a series of 90 cases.

It has been found essential to administer relaxants to obtain adequate operating conditions in all upper and most lower abdominal cases.

The relaxant used in 50 cases was d-tubocurarine hydrochloride. It was found that marked respiratory depression always accompanied a degree of relaxation which satisfied the surgeon.

This amount of respiratory depression might be expected to produce anoxia and carbon dioxide retention.

In 10 cases which did not receive aided respiration clinical cyanosis was not observed, and it was assumed that no anoxia was present. The following points were, however, noted:

(1) A rise of blood pressure ranging from 5mm to 50mm of mercury occurred after the administration of the relaxant.

(2) There was a considerable increase of oozing from the operation site.

(3) The veins of the mesentery were seen to be nearly as pink as the arteries. This was taken to indicate that the mesenteric arterio-venous shunt mechanism was active despite the autonomic blockade produced by hibernation anaesthesia.

It was thought that carbon dioxide retention might be responsible for the initiation of the arteriovenous shunt mechanism.

Postoperatively, 2 of these cases developed a localized pulmonary collapse. Both were hysterectomies maintained in a moderate Trendelenberg position for 45 and 60 minutes respectively. The pulmonary collapses were probably due to inadequate ventilation during the operation.

It was then decided that controlled respiration should be used in all cases where the respiration was depressed in the hope of:

(1) Eliminating CO_2 retention and exploiting fully the potential "dry field" of hibernation anaesthesia.

(2) Preventing postoperative pulmonary complications.

Controlled respiration with 100 per cent oxygen is unnecessary and the elimination of the nitrogen from the lungs predisposes to pulmonary collapse. Dilution of the oxygen with nitrous oxide is a common practice. The nitrous oxide serves no useful purpose as anaesthesia is sufficient already.

It was decided that controlled respiration using air was the answer. A cylinder of compressed air was fitted with an Adam's reducing valve and rotameter intended for use on an oxygen cylinder. It was calculated that about 10 per cent more air was delivered than shown by the flowmeter. The delivery tube from the air cylinder was connected by a T-junc-

tion (an Ayre's T-piece was used) to the delivery tube of a Water's cannister, and with this arrangement air, or air enriched by oxygen, can be given.

Full controlled respiration has been used in 37 abdominal cases to date. In 9 cases where the blood pressure dropped below 90 systolic the air was enriched with oxygen to give a calculated 40 per cent oxygen. In the other 28 cases pure air was used. A flow rate of 5 litres/min was employed with the valve slack enough to allow excess to escape. The blood pressure remained stable in the majority of cases.

The amount of bleeding has been minimized. A most striking observation is that bleeding is much reduced even in those cases whose blood pressure remained about normal.

Observation of the mesenteric vessels has shown that the veins appear much darker than the arteries indicating the maintenance of a normal circulatory pattern.

There have been no postoperative pulmonary collapses in this series to date.

Air has also been used in 18 head and neck cases where the patient's respiration was adequate and not embarrassed by relaxants.

These patients had been hibernated and it was thought essential to have control of the airway and to have them connected to an anaesthetic machine.

They were intubated and connected to the Y-piece of a circle absorber. The expiratory tube was disconnected from the machine employing Bullough's technique. The lead from the air cylinder was connected to the inlet of the absorber and a flow of 7 litres/min used. The patients were maintained in a 10 degrees head up position and bleeding was minimal.

The use of air in this series has enabled the advantages of hibernation anaesthesia and relaxants to be fully exploited with the minimum physiological upset to the patient. This has produced first-class operating conditions and excellent postoperative recovery.

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REGISTRAR'S PRIZE

Royal Society of Medicine: Section of Anaesthetics

Through the generosity of an anonymous donor the Anaesthetic Section of the Royal Society of Medicine is able to offer a prize of £30 for the best paper submitted by those of Registrar Status in the N.H.S. working in a clinical anaesthetic department. Fellowship of the Royal Society of Medicine is not necessary for entry. The subject will be of the author's choice but must be connected with anaesthesia. For this first award all papers must be submitted by April 30, 1956. Further details and rules of the Prize can be obtained from the Honorary Secretary, Anaesthetic Section, Royal Society of Medicine, 1 Wimpole Street, London, W.1.

Brit. J. Anaesth. (1956), **28**, 126

PROMETHAZINE IN GENERAL ANAESTHESIA

BY

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INTRODUCTION

THE introduction of the phenothiazine derivatives into anaesthetic practice has stimulated much research into their uses and abuses in modern anaesthesia. The early Continental approach to the problem was so shrouded in polypharmacy as to make it impossible to ascribe any part of the results obtained to any given drug.

More recently, reports have been made of clinical series in which chlorpromazine, promethazine and pethidine have been the only drugs used prior to the induction of anaesthesia. Both chlorpromazine and promethazine are relatively new drugs and Burn (1954) asks whether "since from pharmacological evidence, there is not very much to choose between these substances as far as their central action is concerned, would it not be possible for observations to be made in patients using only one substance at a time?"

Circumstances have not permitted the controlled conditions advocated by Burn, but in this paper a report is made on the use in anaesthesia of a mixture of pethidine and promethazine without the addition of chlorpromazine.

PHARMACOLOGY OF PROMETHAZINE

Promethazine shows in varying degrees the well-known properties common to the phenothiazine derivatives. It belongs to the antihistaminic group and shows marked anti-emetic properties. Promethazine has a slight local anaesthetic effect and has an action similar to quinidine on cardiac muscle (Hutcheon, 1953). It also tends to paralyse skeletal muscle and it prolongs the effects of curarization (Burn, 1954).

Its effect in lowering body temperature is much less marked than that shown by chlorpromazine (Burn, 1954).

Promethazine has an undoubted sedative effect and Winter (1948) showed this to be allied to a potentiation of barbiturate-induced sleep.

Howarth and Owen (1954) investigated the effects of promethazine on the human cardiovascular system during cardiac catheterization. Following promethazine injection, there was a mild tachycardia but the systolic blood pressure remained unaltered. There were no electrocardiographic changes.

Reckless (1954) has noted a "paradoxical potentiation" by promethazine of the respiratory depressant effects of pethidine and morphia. This effect is less reliable with promethazine than with chlorpromazine.

Promethazine has a marked relaxing effect on the bronchial musculature, especially in asthmatic patients and

Dinnick (1954) has remarked on its usefulness in anaesthesia for such patients.

A short series of fifty cases is presented here, tables I and II respectively showing the operations performed and the age distribution of the patients.

TABLE I

Types of operations performed with promethazine and general anaesthesia in fifty cases.

Inguinal hernia	3
Hemicolectomy	2
Appendicectomy	2
Umbilical hernia	1
Incisional hernia	1
Varicose vein ligation	1
Laparatomy	1
Partial gastrectomy	10
Radical mastectomy	3
Cholecystectomy	5
Cervical sympathectomy	1
Prostatectomy	7
Bilateral ureteric transplantation	2
Total cystectomy	1
Intestinal obstruction (internal strangulation)	2
Nephrectomy	1
Synchronous combined excision of rectum	4
Closure of faecal fistula	1
Transthoracic total gastrectomy	1
Closure of colostomy	1

TABLE II

Age distribution of the fifty patients operated on under general anaesthesia after promethazine injection.

Age (years)	No. of patients
10–20	1
21–30	5
31–40	3
41–50	9
51–60	10
61–70	16
71–80	4
81–90	2

There was no selection, the only criteria being adequate time for a full pre-operative assessment and careful follow-up.

Premedication was administered one hour before the operation. It consisted of pethidine and atropine in thirty-one cases, opiate and atropine in fourteen cases, and pethidine, promethazine and atropine in five cases. Promethazine was incorporated in the premedication in patients who suffered from chronic chest conditions associated with bronchospasm. In these cases the bronchospasm was markedly relieved on their arrival in the anaesthetic room.

Atropine was included in all cases in an attempt to keep the series comparable with previous experience without promethazine.

On arrival in the anaesthetic room the patients were given an intravenous injection of a mixture of pethidine and promethazine. The mixture contained 100 mg of pethidine and 50 mg of promethazine made up to 10 ml with water. This mixture was injected slowly, whilst observing the effect on the patient. The majority of cases were given 40–50 mg of pethidine and 20–25 mg of promethazine.

Within 10 minutes of the initial injection, the patients, after passing through a phase described by many of them as a "floating sensation", became drowsy and the majority fell asleep. At this stage, the blood pressure remained unaffected but the pulse rate was raised, usually by about 10 to 20 beats per minute. There was a noticeable pallor of the face, but no increase in sweating, and the temperature remained unchanged.

Anaesthesia was then induced with a minimal dose of thiopentone—forty out of fifty cases needed less than 350 mg. If the patient was to be intubated, this was followed by 40 mg of suxamethonium chloride. Anaesthesia was maintained with gas and oxygen in a ratio of 4 : 2. If a relaxant was used during the operation, respiration was assisted or controlled, using a circle absorber.

For abdominal surgery, d-tubocurarine or gallamine was used to provide relaxation. In some patients the dose of relaxant needed was found to be smaller than one would have expected had promethazine not been used. This was not invariable, but it was found advisable to proceed cautiously with relaxants, observing the effect of a preliminary injection of 7.5 mg of d-tubocurarine or 40 mg of gallamine.

In all cases, however, the dose of thiopentone needed for adequate anaesthesia was markedly reduced. In forty of the fifty cases the operation was completed using less than 500 mg of thiopentone.

During operation the initial rise in pulse rate was maintained—the rate was usually between 100 and 115 beats per minute. In the absence of severe haemorrhage the blood pressure remained steady. If the patient suffered a rapid loss of blood, the blood pressure fell, returning to its pre-haemorrhagic level on the loss being made up.

POSTOPERATIVE COURSE

Within a few minutes of ceasing the nitrous oxide administration, the patients regained consciousness up to a point where reflexes were present, and within 30 to 45 minutes, all the patients responded to stimuli and opened their eyes when spoken to. Most of them were, although apparently conscious, quite unconcerned and remained in this happy state for 8 to 12 hours. One patient became extremely restless on return to the ward. She had undergone a radical mastectomy and her restlessness may have been related to distress due to tight strapping of the chest wall. She settled down quickly on 50 mg of pethidine.

Very little analgesia was found necessary or even advisable in the first few postoperative hours. One patient, aged 64, was given 100 mg of pethidine 3 hours after operation for cholecystectomy. She fell asleep very rapidly and her respiration rate fell to 4 per minute; she recovered after an injection of nalorphine. Since this occasion it has been made a rule that no patient be given more than 50 mg of pethidine or $\frac{1}{3}$ grain (7 mg) of morphia at one dose if promethazine has been used during anaesthesia.

There were no serious respiratory complications in this series despite the fact that nine cases were labelled pre-operatively as suffering from chronic bronchitis not likely to be further improved by physiotherapy.

The incidence of nausea and vomiting was as follows: five patients admitted on questioning to slight nausea but no vomiting; six patients vomited at least once during the first 24 hours, five of these patients had undergone major abdominal operations, but the sixth vomited 3 hours after a difficult and prolonged radical mastectomy.

These figures are somewhat disappointing in view of the anti-emetic properties attributed to promethazine. It may be significant that in four of the patients, vomiting occurred between 12 and 24 hours postoperatively when the promethazine effect had presumably worn off. It is hoped to follow up a much larger series from this aspect.

COMMENT

This preliminary investigation indicates that the use of pethidine and promethazine without the addition of chlorproma-

zine may have a place in everyday anaesthesia. It appears to be of especial value in major surgery in elderly and bad-risk cases. It is a clinical impression that the technique has the advantage of reducing the dose of thiopentone needed for anaesthesia without lowering the patient's blood pressure. Postoperatively, there is a rapid return of the patient's reflexes, but the degree of " dissociation " produced by the promethazine ensures a comfortable recovery in the first few postoperative hours.

ACKNOWLEDGMENT

My thanks are due to the Consultant Anaesthetic Staff of the Whittington Hospital for their co-operation and encouragement.

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BOOK REVIEW

Clinical Analgetics. By Professor E. G. Gross (University of Iowa) and M. J. Schiffrin, Ph.D. Published by Charles C. Thomas. Price 21*s*. 6*d*.

This is another of the thin black books published simultaneously in America and Canada by Thomas and the Ryerson Press and in this country by Messrs. Blackwell of Oxford. The name " Analgetics " will probably be new to English readers but the authors define it as " Those materials which when administered provide relief from pain by means other than reduction or removal of the causative factor." At first sight this definition would appear to embrace such materials as hot-water bottles, mustard plasters, and setons, though psycho-analysis, hypnotism and Christian science would be ruled out as being not material. As none of these things is mentioned in the subsequent text it is clear that the authors did not so intend it. As an illustration of what they do mean they instance the action of morphia which removes the pain of biliary colic by its influence on nerve centres while amyl nitrite alleviates it by the reduction of intrabiliary pressure. So morphia is included in this somewhat exclusive circle of " Analgetics " and amyl nitrite is left out. They have also adopted the term " Opioid " following the suggestion of Messrs. Acheson and Pfeiffer who in their turn may possibly have had in mind the well-known " Tabloid " which many years ago Messrs. Burroughs Wellcome invented for their products which resembled what had hitherto been looked upon as tablets. The term " Opioid " means synthetic compounds something like opium.

Of the seven chapters of which this small book consists no less than four are devoted to opium, opioids, and their antagonists. The practice of putting the structural formula at the head of the account of each drug is to be commended. It gives the student an idea of the relationship of drugs and how variation in structure influences pharmacological activity. The account of the action of nalorphine is at variance to that given by Payne, who found that nalorphine produced " No marked antagonism to morphine, except a transient stimulation of respiration, that many of the effects observed were both unpleasant and prolonged." The discrepancy between the two descriptions may be accounted for by the different circumstances in which this drug was used.

On pages 20, 21, and 22 there is a long list of proprietary medicines sold in the U.S.A. which contain one or more of the following: salicylates, paraminophenols, pyrazolons other than aminopyrine, and aminopyrine. It may be of value to the American but is useless for this country, as there is scarcely a proprietary name in this very long list that we have ever heard of. Not only is this long list of medicines American but the list of references is, as usual, almost entirely American.

A little note at the end of the book says, " It is the publisher's desire to present books that are satisfactory as to their physical and artistic possibilities." In this they have certainly succeeded.

E. Falkner Hill

Brit. J. Anaesth. (1956), **28**, 130

CAESAREAN SECTION: A METHOD OF ANAESTHESIA

BY

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CAESAREAN SECTION carries a certain maternal and infant mortality for both of which blame is on occasion cast on the anaesthetic. In the mothers' case one of the major sources of trouble is vomiting during anaesthesia. In the case of the child, the anaesthetic drugs reach the infant's circulation and may delay the initiation of respiration.

In recent years muscle relaxants have been increasingly used to overcome these hazards and in addition provide the adequate relaxation demanded by the present-day surgeon. The use of curare as an adjuvant to general anaesthesia for Caesarean section was described by Whitacre and Fisher (1945) and there have been several subsequent reports.

Gray (1947) employed an induction with d-tubocurarine 15 mg, thialbarbitone 300 mg, and maintenance with cyclopropane using aided respiration. No airway was employed as it was suggested that its use would precipitate vomiting. Induction was carried out in the operating theatre when the surgeon was ready to commence operating. A similar method was used by Corbett and Thomas (1949) who reported its use in 100 cases, and by Davenport (1951) in 210 cases.

Climie (1950) recorded 112 cases of Caesarean section using an induction with thiopentone followed by d-tubocurarine 10–15 mg or gallamine 80 mg, and maintenance of anaesthesia with nitrous oxide and oxygen in the ratio 3: 1, with assisted respiration. Cyclopropane was given if patients showed signs of too light anaesthesia.

Thomas and Gibson (1953) used thiopentone 250 mg, or thialbarbitone 500 mg, followed by cyclopropane. Following this induction the patient's stomach was emptied with a stomach tube, gallamine was then injected and anaesthesia maintained with nitrous oxide and oxygen in the ratio 2: 1.

Similar methods to these were used by the writer in anaesthesia for Caesarean section. The results as evidenced by the condition of mothers and babies were on the whole satisfactory, but certain disadvantages were noted. There was occasional vomiting or regurgitation at induction or during the course of operation, and delay in commencement of respiration by the baby, particularly after previous foetal distress, or when the babies were premature.

In addition, these methods assumed that the delivery would be completed rapidly after induction in order to avoid accumulation of depressant anaesthetic agents in the infants. In practice, it was found impossible to achieve rapid delivery in all cases, particularly those with ante-

partum haemorrhage requiring preliminary vaginal examination under anaesthesia.

It was felt that these disadvantages could be overcome by avoiding the use of barbiturates, by employing a cuffed endotracheal tube in all cases and by the use of controlled respiration. The method evolved has been used in 100 cases of Caesarean section.

METHOD

Premedication consists of atropine 1/100 grain (0.6 mg) given either by intramuscular injection, half an hour before operation or by intravenous injection immediately prior to operation.

Anaesthesia is induced, in the anaesthetic room, with cyclopropane and oxygen at the flow rate of 700 and 500 ml per minute respectively. This is maintained until the patient's respirations are regular and steady and her limbs relaxed; d-tubocurarine 25 to 30 mg is then given intravenously and when apnoea occurs the patient is inflated for a short period by manual compression of the rebreathing bag, following which a cuffed endotracheal tube, size 8 or 9, is passed. Anaesthesia is maintained with nitrous oxide and oxygen in the ratio of 1:1, using controlled respiration.

The patient is then transferred to the theatre. The carbon dioxide absorber is removed from the circuit when the peritoneum is opened in order to ensure that the carbon dioxide concentration in the foetal blood is not below normal at birth.

Usually the mother remains apnoeic until the baby is delivered, but it has been a feature of these cases that, despite the initial high dose of d-tubocurarine, fairly full spontaneous respiration has returned within five minutes of the delivery. It is then convenient to add cyclopropane or ether to the closed circuit and allow the operation to finish either with the mother breathing spontaneously, or with assisted respiration. Alternatively apnoea may be restored by a short period of hyperventilation and controlled respiration continued. In all cases the patient is given atropine 1/50 grain (1.3 mg) and neostigmine 2.5 mg intravenously at the end of operation, in order to ensure full recovery from the effects of the d-tubocurarine. Following this the endotracheal tube is removed. Most patients are conscious by the time they are ready to leave the theatre.

MATERNAL RESULTS

The induction described has been pleasant and rapid. Occasionally a patient has requested "the needle" but has readily agreed to inhalational anaesthesia when it has been explained that this was for the benefit of the baby. There have been no cases of vomiting, although one patient regurgitated a small amount after the start of the induction, but whilst she was still conscious. The use of a cuffed tube and controlled respiration have ensured adequate ventilation and eliminated the dangers of regurgitation during operation.

The maternal mortality was nil. One patient who had a cold at the time of operation developed bronchopneumonia on the following day and four other patients developed small areas of atelectasis. All these cases recovered within a few days with chemotherapy and physiotherapy.

Collapse occurred in one case shortly

after induction of anaesthesia. This patient had had an antepartum haemorrhage two hours before undergoing an emergency Caesarean section. Her blood pressure immediately before induction was 100/60 and pulse rate 100, and one half-pint of blood (280 ml) had been given. Ten minutes after induction, her pulse became imperceptible and her face was pale, cold and clammy. Methylamphetamine 15 mg was given intravenously and the rate of blood transfusion was increased. These measures rapidly restored her pre-operative blood pressure and the baby, when delivered fifteen minutes after induction, reacted vigorously two minutes later.

INFANT RESULTS

The infant mortality was represented by four neonatal deaths from a total of 102 births. The four neonatal deaths are listed as follows:

(1) Baby weighed 3 lb. 14 oz. (1.8 kg). Died 8 hours after delivery. Postmortem examination showed hyaline membrane and pulmonary atelectasis. Emergency Caesarean section was performed at 30 weeks for severe bleeding from a placenta praevia.

(2) Baby weighed less than 2 lb. (0.9 kg). Died 2 hours after delivery. Its mother had been bleeding off and on for 4 weeks prior to having a fairly severe haemorrhage on the day of operation. The period of gestation was thought to be about 28 weeks.

(3) Baby weighed 3 lb. (1.4 kg). Died 24 hours after Caesarean section at 28 weeks for essential hypertension (blood pressure 180/100) and foetal distress.

(4) Baby weighed 5 lb. (2.3 kg). Died 2 days after delivery. The child reacted strongly one minute after delivery, but despite strong respiratory efforts, it appeared to be unable to ventilate its lungs adequately, and each inspiration was accompanied by a marked indrawing of its chest wall. Postmortem examination revealed hyaline membrane and atelectasis. The mother had severe diabetes and elective Caesarean section was carried out at 36 weeks.

The average time taken for the infants to commence breathing or crying after full delivery from the uterus was 32 seconds. Figure 1 shows that 65 babies started to breathe within 30 seconds of delivery whilst the longest time taken was 2 minutes 40 seconds. In 16 infants, the initial respirations consisted of occasional gasps, but all were crying or breathing regularly and strongly within 7 minutes of birth.

Resuscitative measures were practised on the 19 infants who did not react after one minute following birth. These con-

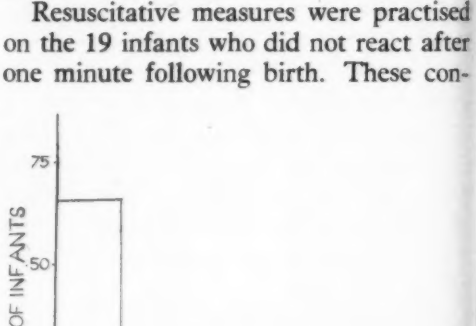

FIG. 1

Showing the time taken for initiation of respiration in 102 infants delivered by Caesarean section.

sisted of intranasal oxygen and pharyngeal suction in 18 cases. Five in addition received an intramuscular injection of lobeline. One infant was intubated and oxygen was administered by intermittent positive pressure.

DISCUSSION

It has been demonstrated by Hellman et al. (1943) that when barbiturates are injected intravenously, little reaches the foetus in the first 5 minutes, but within 10 to 12 minutes the concentrations in the maternal and foetal blood are equal. Thus, when barbiturates are used for induction of anaesthesia for Caesarean section, in order to deliver the child before the drug crosses the placental barrier, it is necessary, either to induce anaesthesia when the mother is in the operating theatre and the surgeon waits "knife in hand", or to rush the patient into the theatre for a rapid preparation after induction in the anaesthetic room. In either case the operation must be rushed and, even so, it is not always possible to complete the delivery within a specified time.

In the present series, the inductions were carried out in the anaesthetic room. The average time taken between induction and start of operation was 8.7 minutes and a further average time of 9.9 minutes was taken from the start of operation to delivery of the baby. The minimum and maximum times for these periods are shown in table I. The minimum time for the period from induction to delivery was 9 minutes, whilst the maximum time was 35 minutes. There was a considerable delay in the start of operation in those cases which required a preliminary vaginal examination to confirm the presence of placenta praevia. There was no correlation between these times and the duration of apnoea in the infants.

TABLE I
Time taken for stages in 100 Caesarean sections

	Time in minutes		
	Minimum	Maximum	Average
Induction to operation	4	20	8.7
Operation to delivery	4	19	9.9
Induction to delivery	9	35	18.6

During even the minimum time taken for delivery the cyclopropane used for induction would be largely eliminated, and as the mothers were maintained only on nitrous oxide and oxygen there appeared to be no great need for rapid delivery, as the infants were not absorbing depressant volatile or intravenous anaesthetic agents. This factor was felt to be a great advantage as it enabled a careful incision and extraction of the baby to be carried out without undue haste.

The dose of d-tubocurarine used in these cases was higher than that used in other series reported, but in no case was there evidence of curarization of the infants nor sensitivity in the mothers. Most of the infants cried lustily immediately after delivery. Delay in the onset of crying or regular full respiration was confined mainly to those babies whose mothers had previously received pethedine and to those babies who had previously shown signs of foetal distress, but even these infants did not appear depressed, once crying or regular respiration was established.

In general, most people are agreed that d-tubocurarine does not cross the placental barrier to any extent. Pittinger and Morris (1953a) have shown that when curare is injected in high doses into the

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In general, most people are agreed that d-tubocurarine does not cross the placental barrier to any extent. Pittinger and Morris (1953a) have shown that when curare is injected in high doses into the

uterine arteries of pregnant dogs, it can subsequently be detected in the foetal circulation, but the same workers (1953b) have not been able to detect it in the cord blood of human infants after heavy curarization (apnoeic doses) of the mothers during labour.

CONCLUSION

The hazards of general anaesthesia for Caesarean section can be reduced by avoiding the use of barbiturates and the prolonged administration of depressant anaesthetic agents, and by utilizing controlled respiration with a cuffed endotracheal tube.

The method described provides safe anaesthesia for the mother and does not depress the infant. In addition it provides good working conditions for the surgeon and enables the operation to be conducted without undue haste.

ACKNOWLEDGMENT

I wish to thank Dr. D. C. C. Stark, Anaesthetist, Maryfield Hospital, for his valuable assistance in accumulating data for this paper.

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CORRESPONDENCE

THE USE OF DIPHTHONGS

Sirs,—Anaesthetists who write textbooks and papers are developing a conditioned reflex. Sirs, please implant in their higher centres the inhibitory knowledge that " oe " does not invariably follow " pn ". If you do not, there is worse to come. From hypercapnoea, hypocapnoea and acapnoea, hypoxoea and anoxoea will logically follow. And from these, with other horrors unnamed, asphyxoea, anaemoea, uraemoea, arrhythmoea, dementoea.

HAROLD YOUNGMAN
Cambridge University

INTRA-ARTERIAL THIOPENTONE

Sirs,—When considering methods whereby this tragedy may be avoided, Dr. Forrester and Dr. Saunders (*Brit. J. Anaesth.*, **27**, 594) recommend that the site of the proposed injection be carefully palpated to detect any pulsation before the " tourniquet " is applied. This is of paramount importance, even though, as they point out, arterial pulsation may not always be detected.

The strong grip of a keen assistant is a well-known cause of arterial occlusion, but the purpose of this letter is to draw attention to another, admittedly uncommon, situation when arterial pulsation may be absent in part of the forearm.

Before venepuncture it is customary for the arm to be held over the side of the trolley with the elbow fully extended; however, the elbow joint can be hyperextended in a minority of people—usually children—and this is readily done under these circumstances.

This is usually of little significance, but I have observed that if this hyperextension occurs in an arm which also has an abnormal superficial ulnar artery, then the latter may be occluded where it passes over the common flexor origin.

It is therefore advisable to ensure that the elbow joint is not hyperextended when the forearm is examined for arterial pulsation.

O. P. DINNICK,
Middlesex Hospital, London, W.1

Brit. J. Anaesth. (1956), **28**, 135

AN ASEPTIC LUBRICANT DISPENSER FOR ENDOTRACHEAL TUBES

BY

E. K. HILLARD

Department of Anaesthetics
Welsh National School of Medicine, Cardiff

NORMALLY the lubricant so necessary for endotracheal tubes is supplied in squeeze tubes or jars. It has therefore to be smeared on a swab or finger so that it can be applied to the tube. Neither method is elegant or clean.

The illustration (fig. 1) shows a lubricant dispenser for K.Y. and similar jellies which has been developed in this department at the request of Professor Mushin. It has been in use for a considerable period and has given very satisfactory service.

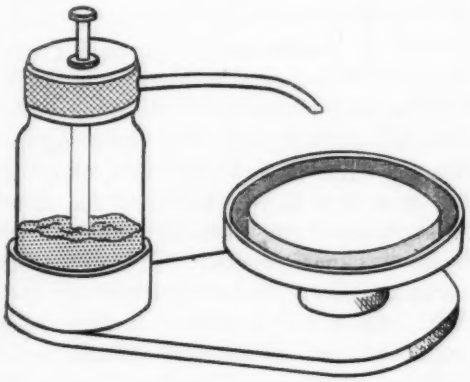

FIG. 1

A push on the plunger deposits lubricant on the platform, on which the endotracheal tube is then rubbed to and fro. The lubricant is thus untouched by finger or swab. Excess lubricant on the tube can be removed on the edge around the platform. The shallow circular groove pre-prevents soiling of the rest of the device. After each use the platform is lifted from its socket and cleaned. The whole instrument is made from transparent plastic with the exception of the glass bottle.

ACKNOWLEDGMENT

I have to thank Messrs. County Laboratories Ltd., for permission to copy the plunger mechanism in their Brylcreem dispenser.

ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

JOHN SNOW, M.D.

Licentiate of the Royal College of Physicians

(*Continued from page* 96)

The flow, however, almost instantaneously ceased, and Dr. Rooke, who kept his finger on the man's pulse, found that cease at the same moment. Respiration appeared to cease almost instantaneously with the heart's action. Regular respiration at least did; for, while we were looking at the man's face, he fetched one or two sigh-like inspirations. The ribs and abdomen were compressed, so as to induce inspiration and expiration; the lungs were inflated by blowing through the nostrils, the larynx being compressed against the spine, and, for three or four minutes, upon our efforts being suspended, the man occasionally took an inspiration; on one occasion three or four in succession, so as to make us flatter ourselves that he would come round. . . . It is worthy of remark that, for a long time after spontaneous respiration had ceased, the lips retained a florid colour. The muscles were all relaxed, and the veins on the side of the neck turgid."*

At the inspection of the body next day, the vessels of the dura mater, and those on the surface of the brain, were gorged with fluid blood. The lateral sinuses also afforded a flow of dark-coloured blood. There was a considerable quantity of serous fluid in the cavity of the arachnoid and in the spinal sheath. The substance of the brain was very soft. (The weather was warm.) The lungs were of a dark purple colour posteriorly, and much loaded with fluid blood and serum, but were everywhere crepitant and healthy. The external surface of the heart was covered almost entirely with fat; in some parts to a considerable thickness. There were two fibrinous spots on its surface. No fluid in the pericardium. The venæ cavæ were full of fluid blood. On removing the heart, a white fibrous coagulum, about as big as a walnut, was found in the commencement of the pulmonary artery. The heart was uncontracted, and the cavities contained a very small quantity of dark fluid blood. The walls of the right ventricle, and of the left auricle, were thinner than natural. Some portions of the substance of the heart were paler than natural:—"In these paler portions of the muscular substance, the fibres had, for the most part, lost their striated aspect, and had become converted into a fine granular material contained in the sarcolemma. Here and there a minute oil-globule could be observed in the muscular fibrillæ, but nowhere did this amount to fatty degeneration."

* Medical Times, 1851, vol. ii, p. 98.

In this case all the precautions appear to have been taken which are possible in making a patient insensible with undiluted chloroform, administered on a handkerchief; and the case, therefore, strongly confirms the proposition that chloroform cannot be administered in this way with perfect safety.

The patient was apparently in the most satisfactory condition at the conclusion of the inhalation and yet, a few seconds afterwards, the heart suddenly ceased to beat, from the effect, as we must conclude of that portion of vapour which was in the lungs at the moment when the inhalation was discontinued.

Case 24 occurred in October, 1851, at Chipping Norton, Somerset, to a patient of Mr. Farwell named Elizabeth Hollis, and aged 37. No one observed the manner in which the breathing and circulation ceased, and, as the patient was in a state of extreme debility, it is not quite certain that the chloroform was the sole cause of death. It was administered to prevent the pain of removing the fæces, which became impacted in the rectum on account of extensive cancerous disease of the uterus and vagina. The surgeon reports that "the time occupied in the inhalation was about eight or nine minutes; quantity inhaled 10½ drachms, half a drachm at a time, allowing her frequently to breathe the atmospheric air. She spoke to me during this period. When I found that her arm fell after being raised, I proceeded to and accomplished the operation. At this time she was not inhaling. I then, as I always do, wetted the face with a sponge, with a view of washing off any remaining chloroform from the nose and lips, when, to my surprise, I found that she had ceased to breathe, and all attempts to restore her were in vain. . . . When I commenced the operation, the pupil was contracted, and the conjunctiva slightly red. After death, the pupil was very dilated, and the countenance extremely pallid."* There was no inspection of the body. This patient had inhaled chloroform on two previous occasions for a similar operation.

Case 25 occurred in St. Bartholomew's Hospital, on March 17, 1852. Thomas Hayward, aged 23, was suffering from aneurism by anastomosis, occupying the right ear and its neighbourhood. He had inhaled chloroform on the 14th of the previous month, whilst Mr. Lloyd placed ligatures on the temporal artery and some other arteries supplying the tumour; and it was with a view to tie an additional artery, situated between the mastoid process and the ramus of the jaw, that chloroform was again administered.

"The chloroform was some of the same, and the apparatus employed for its administration precisely similar [alluding to the former occasion]. It was administered by one of Mr. Lloyd's dressers, who well understood, and had great experience in its use. A gentleman of great experience, who had been for years at the hospital, and two years house-surgeon, was watching its effects, and marking the state of the pulse. Other gentlemen were assisting, and also on the look out.

"In from five to ten minutes the usual effect was produced, the patient having previously struggled much. The operation

* Medical Times, 1851, vol. ii, p. 620.

was then commenced; but no sooner had Mr. Lloyd cut the skin, than it was stated that the pulse had suddenly ceased. The chloroform was at once removed; but in a few seconds, the patient had ceased to breathe, and no pulsation could be felt at any of the arteries or the heart.

"Artificial respiration, as well as percussion and compression of the different parts of the body, were immediately employed with energy; and, after continuing the means for a short time, the circulation was observed to be returning, and the act of respiration was several times performed. The state of inanimation, however, speedily returned; but, by the employment of the same means as before, with the use also of galvanism, the circulation and respiration were again restored. Quickly, however, the patient fell into the same state as at first, but was again restored by the same means.

"In a few minutes the state of inanimation again returned, when the external jugular vein, which on the right side was very turgid, was opened, and tracheotomy was performed, and the lungs inflated. The patient was also placed in a warm bath, at the temperature of 104°, artificial respiration being kept up all the time. All, however, was of no avail."*

At the examination of the body, the following are amongst the appearances noted. "The venæ innominatæ and vena cava superior were full of blood, and probably would have been distended, but that two or three ounces of blood had flowed into the coffin from the opening made into the external jugular vein. The right auricle and ventricle were distended with blood, and would probably have been more so but for the escape of blood mentioned above. The left auricle and ventricle contained very little blood; the left ventricle was perfectly contracted in the rigor mortis. The heart was of full size. It appeared in every part natural in its texture, and as if it had possessed full power. Its valves also were all healthy; neither could any disease be found in any of the chief blood-vessels within the chest. All the blood, however, was fluid, and it remained without coagulation after its escape from the heart and vessels. It had also a brownish purple hue, much like that which is commonly observed in the spleen: none of it, when thinly spread out, presented the ordinary dark, black, or crimson hue of venous blood. Both lungs were attached by old adhesions about their apices and posterior surfaces but these were of small extent. Their texture was healthy, but they appeared more than usually collapsed and dry. Their blood-vessels were not over filled."*

In this case, every precaution seems to have been taken, except that one which is most essential of all, of regulating the proportion of vapour in the inspired air. It had always been made a great point in St. Bartholomew's Hospital to attend to the pulse very carefully,† and on this occasion it was closely examined, but only, as in some other cases, with the result of being able to note the moment when it suddenly ceased.

With regard to the return of the circulation, which is mentioned in the report as having occurred on three occasions,

* Medical Times and Gazette, vol. i, p. 293.

* Medical times and Gazette, p. 318.

† See a clinical lecture by Mr. Stanley, Med. Times, Nov. 22, 1851.

together with the breathing, during the efforts at resuscitation, I understood from inquiries I made of a gentleman present, that this was judged of from the red colour returning to the face and lips, but the pulse and sounds of the heart were never distinctly perceived after they first ceased. The respiration may cause the colour to return to the face without a true circulation, as I have seen whilst inflating the lungs of still-born children; for if a portion of red blood be mechanically displaced from the lungs by the motion of the chest, it will be propelled by the contractility of the arteries, which continues for some time after death.

Case 26 is related by Dr. Majer, of Ulm.* It occurred on June 27th, 1852. The patient, Madame W., was 32 years of age, and of good constitution. She was in very good spirits, and was only waiting the operation of having a tooth extracted, before going to dinner. It was stated that only twenty or twenty-five drops of chloroform were put on a sponge, which was surrounded by a handkerchief. After four or five inspirations, the operator inquired if his patient did not feel a singing in the ears. She replied with a trembling and thick voice. At the same time she stretched out her limbs, the face became bluish, the eyes haggard, the head and the arms fell —she was dead. The patient's husband said, that the time between the inhalation and death was so short that one could scarcely have said Yes or No.

An examination of the body was made twenty-five hours after death. Putrefaction had commenced, and the body was not rigid. The vessels of the membranes of the brain were gorged with blood containing many bubbles of air. The heart was soft and flaccid; the coronary vessels were engorged with blood and air; the cavities of the heart contained air, but little blood. The lungs were congested at the inferior parts.

Case 27 took place at Melbourne, Australia. The name of the patient was Mr. John Atkinson, but his age is not stated. Dr. Thomas, who was about to operate for fistula *in ano*, said: "Before administering the chloroform, I asked the deceased particularly if he had ever suffered from any serious illness, to which he replied in the negative. I also inquired whether he had been subject to cough or palpitation, and he answered that, some time ago, he had suffered slightly from cough. The pulse was good, and Mr. Barker proceeded in the usual manner to administer the chloroform, which shortly produced convulsive twitchings of the muscles. I then went to the door to request the nurse to send up some person to assist in holding the patient in a proper position for the operation, and I returned to the bed, and poured a little more chloroform on the handkerchief; when it was applied to the face, I heard him splutter at the mouth; the chloroform was instantly discontinued, but the patient suddenly expired. We tried all the means usually resorted to in other cases of suspended animation, but without effect. I had frequently used the same chloroform in other cases. It was not more than a minute after the first application of chloroform that death occurred. About a drachm had been poured on the handkerchief."

* Gaz. Médicale, 1852, p. 630, from Medicinisches Correspondenz Blatt.

At the examination after death, " there was considerable serous effusion into the pericardium, and the heart itself was larger and more flabby than usual. It was hypertrophied, and there was dilatation of the cavities; the lungs were healthy, and there was a slight appearance of disease about the liver, such as is observed in persons addicted to intemperance."*

Case 28. On August 10th, 1852, a Mr. Martin, a cattle dealer, died near Melrose, in Scotand. after inhaling chloroform for the application of potassa fusa to some ulcers of the leg. Dr. W. M. Brown, who relates the case, says: —" Before proceeding to apply the caustic I gave him chloroform. He was not easily affected by it, and struggled a good deal. After beginning to apply the caustic I found he was not sufficiently insensible to pain, and gave him a little more chloroform, which had the desired effect. I then proceeded with the application of the caustic, and was just finishing, when I observed a sort of catch in his breathing. I immediately stopped, and, on looking at him, I saw the mouth and eyes open, the breathing irregular, the face pale, the eyes slightly turned upwards, and the pupils dilated." Dr. Brown tried artificial respiration and other means to resuscitate the patient, but without effect. He says, " in a few minutes the man died." The pulse is not mentioned, nor the age of the patient.†

Case 29 took place in the Manchester Royal Infirmary, on December 24th, 1852, during the removal of a malignant tumour of the thigh, by Mr. Jordan. The patient was Henry Hollingsworth, a factory operative. His age is not stated. 'The man was very much excited, struggled and talked fast. The chloroform was administered slowly, and every precaution was taken to prevent any danger, and the medical men remarked two or three times how very long it was in taking effect. He at last became insensible, in about seven minutes at least. Mr. Jordan commenced the operation by an incision into the skin covering the tumour. I was assisting the surgeon when Mr. Heath directed my attention to the patient's face. This was about five minutes after the operation had commenced. I then observed congestion about the face, but there was no stertorous breathing. His pupils appeared almost to have ceased to act. His breathing was becoming exceedingly slow, and he seemed to be sinking fast. I directed the attention of the operator and the other medical men to these symptoms. The operation was then suspended, and means were resorted to for restoring animation, but the pupils had ceased to act, and had become fixed almost immediately. He gave one strong gasp, and then all appearance was dead. In administering the chloroform, successive doses were given until it took effect. Every dose consisted of a drachm, taken, at intervals, in an inhaler."*

The following remark is made respecting the autopsy. 'The post-mortem examination shewed that asphyxia, caused by chloroform, produced the death. There was a congestion both of the brain and lungs." The appearances met with after death from chloroform do not indicate the way in which death has taken place.

* Medical Times and Gazette, 1852, vol. ii, p. 531.
† Monthly Journal of Med., vol. xv, 1852, p. 377.

* Lancet, 1853, vol. i, p. 21.

In animals that are killed by it, the right cavities of the heart are always found filled with blood whether they die suddenly by its direct action on the heart, or more slowly by its effects on the brain, and the breathing ceases before the circulation. The lungs are seldom much congested in animals, whichever be the mode of dying, and the appearances in the head are not unusual. The state of the pulse is not mentioned in the above account of the case; but congestion about the face was first observed, and then it was noticed that the breathing was getting slow. It is sufficiently probable that the breathing ceased on account of the action of the heart being first arrested; but even if the respiration was embarrassed by the action of the chloroform on the brain, it is pretty certain that that agent also acted directly on the heart; for it cannot be supposed that the means used for restoring animation would have failed, if the heart had been acting properly when the breathing ceased.

Case 30 took place on March 19th, 1853, in University College Hospital, London. The subject of it was an unmarried woman, named Caroline Baker, aged twenty-eight. The chloroform was administered with the intention of applying nitric acid to a sloughing ulceration of the labia and vagina. "The chloroform, supposed in the first instance to be about a drachm, was poured on lint about five inches square, and folded four or five times over. After a short time the patient became restless, talked loudly, and threw about her arms. Soon afterwards a partial relaxation of the limbs took place, and she became insensible and pulseless."*

* Lancet, 1853, vol. i, p. 307.

Further symptoms are not given, but it is stated that she sank and died. The breathing is not mentioned, but Mr. Erichsen, who, although not present at the accident to his patient, would be made aware of all that occurred, stated at the inquest, that death was produced by a paralysis of the heart from the influence of the chloroform. Dr. Quain examined the structure of the heart with the microscope, and he "found that organ, particularly on the right side, in a state of fatty degeneration."

Case 31 was communicated to the Society of Surgery of Paris by M. De Vallet, Surgeon-in-chief to the Hôtel-Dieu, d'Orléans. "A soldier of the line, aged twenty-five, apparently in good health, and of strong frame, consulted M. Vallet for a small tumour situated behind the right labial commissure. Before operating, he proceeded to direct the inhalation of chloroform. The patient, fasting, being placed in the horizontal posture, the chloroform (about one gramme) was poured upon a hollow sponge, and applied to the nose, the mouth being left free. At the expiration of a minute, no effect having been produced, four grammes were poured on the sponge, and at the expiration of four minutes, the patient, without having experienced any irritation of the larynx, without having manifested any resistance, without redness of the countenance, and after only a slight period of agitation, fell into a state of insensibility fit for the operation. Scarcely had the incision been made, necessary to expose the cyst, when the patient became pale, respiration was suspended, and he sank into a state of com-

plete collapse. All the usual remedies were tried, and without avail. M. Vallet opened the trachea, and performed artificial respiration with an elastic tube; then an electric current was sent by needles through the region of the heart. The patient died without any sign of reaction.

"Examination of the body. — The vessels of the brain were empty; the lungs were congested with blood, which in some situations was extravasated; the heart was excessively flaccid; there were some soft clots in the right cavities; the left were empty. The stomach was full of gas; the liver, spleen, and kidneys were gorged with black blood."*

* Med. Times and Gaz., 1853, vol. ii, p. 47.

(To be continued)

BOOK REVIEW

Analgesia for Midwives. By Hilda Roberts, M.R.C.S., F.F.A.R.C.S., D.A., D.C.H. Published by E. & S. Livingstone, Edinburgh and London, 1955. Pp. 68; illustrated. Price 10*s*. 6*d*.

This small book, which is dedicated to the National Birthday Trust Fund, is very attractively presented. Besides good photographs and line drawings, it has six coloured plates which have been beautifully executed. The reading matter is well and concisely set out, and clear descriptions are given of the subjects dealt with in the various chapters. In any review there must be honest criticism, but with the exception of one serious mistake on page 23, where the two types of cylinder head are described in the reverse order to what is a fact, there are only a few controversial points to be mentioned.

More could have been said about dealing with fear, which plays such an important part in the success or otherwise of a satisfactory analgesia.

Most Sister Tutors in Maternity Hospitals teach the pupils that pethidine should not be given later than about two to three hours before the birth of the child.

The chapters on the resuscitation of the newborn and the preparation of apparatus and instruments for regional analgesia are rather works of supererogation in a textbook written specially on analgesia for midwives.

This is an excellent book, however, and is recommended to all those engaged in the practice of midwifery. *R. J. Minnitt*

GLASGOW AND WEST OF SCOTLAND SOCIETY OF ANAESTHETISTS

THE third meeting of the 1955–56 session was held in the Royal Faculty of Physicians and Surgeons, 242 St. Vincent Street, Glasgow, on January 19, 1956. The speakers were Dr. H. H. Pinkerton and Dr. A. C. Macdonald, Western Infirmary, Glasgow. Their subject was "Aspects of Carbon Dioxide."

Dr Pinkerton was mainly concerned with the carbon dioxide produced by the patient's metabolism. The use, and abuse, of carbon dioxide in the past to hasten induction of anaesthesia and the "de-etherization" of the patient was mentioned. It was paradoxical that the respiratory depression sought nowadays by most anaesthetists was the cause of acute interest in carbon dioxide and respiratory physiology. This interest had arisen from the anaesthetist's daily use of assisted and controlled respiration. The treatment of some medical conditions, through the extension of modern anaesthetic techniques, was now within the anaesthetist's province, e.g. ventilation of the lungs in respiratory paralysis and the treatment of respiratory acidosis in chronic bronchitis and emphysema.

Controlled respiration, like normal respiration, served a dual purpose—to supply oxygen and get rid of carbon dioxide, the importance of the latter often being overlooked. The results of stimulation of the respiratory centre by excess carbon dioxide were clear enough in the conscious person or in one breathing spontaneously under anaesthesia. In the apnoeic patient an increasing carbon dioxide tension stimulated the respiratory centre and through it the vasomotor and cardiac centres, the clinical indications being sweating, vasodilatation, oozing at the operation site, rising blood-pressure, disturbances of acid-base balance, cardiac arrhythmias, continuing narcotic effects and postoperative collapse. These effects could be produced by hypoventilation. Hyperventilation with lowered carbon dioxide tension was apparently less disturbing and reasonably compatible with our wishes for the anaesthetized case.

The everyday precautions in anaesthesia to avoid carbon dioxide accumulation were mentioned, stress being laid on adequate flow rates and ventilation. Investigations by Schwartz and others had shown that flow rates of 8 litres/minute were required in the semi-open circuit to prevent carbon dioxide accumulation.

Methods of actual measurement of carbon dioxide levels were described, most being too elaborate for everyday theatre use. The carbon dioxide analyser devised by the British Oxygen Company was accurate to within 0.1–0.2 per cent, and some observations made by Dr. Pinkerton with it were described. With patients breathing in the semi-open circuit, flow rates below 7–8 litres/minute were insufficient to prevent carbon dioxide accumulation. In apnoeic patients adequate or overventilation kept carbon dioxide tensions below normal, while easing off or stopping of artificial respiration allowed carbon dioxide to accumulate. In favourable circumstances spontaneous respiration would recommence when (but not until) carbon dioxide levels rose to 5 per cent plus.

There was clearly much scope for work on carbon dioxide levels in our daily anaesthetic methods.

Dr. Macdonald, speaking as a physician, believed that some of the problems of carbon dioxide had relevance to patients requiring anaesthesia and that the help and co-operation of anaesthetists was of great value in some medical cases.

The use of carbon dioxide, usually combined with oxygen, was introduced in 1920 by Yandell Henderson. In 1932 the first warning against carbon dioxide was made by Boothby, this warning being reiterated by Barach in 1940. The use of carbon dioxide by physicians was now almost abandoned.

Carbon dioxide, the first gas used to produce anaesthesia by Hickman in 1820, was toxic. Work done on respiratory physiology as it affected submarines had shown carbon dioxide poisoning to be

the cause of deterioration in men breathing oxygen under pressure. Lovelace, of B.L.B. fame, concluded from experiments that a safe exposure to 5 per cent carbon dioxide was 5 minutes. The toxic effects of carbon dioxide were (1) cerebral (coma and epileptiform fits), (2) cardiovascular (peripheral failure and cardiac arrhythmias), and (3) the "off" effect—collapse, shock and rigors on reduction of the high CO_2 blood level.

Normal control of respiration was by the effect of carbon dioxide on the respiratory centre. There was a carbon dioxide gradient from the tissues to the alveoli of the lung. Raising the alveolar carbon dioxide tension to 7 per cent progessively reduced the carbon dioxide excretion. Alveolar concentration above 7 per cent led to reversal of the gradient and carbon dioxide accumulation resulted.

The application of carbon dioxide to medical cases should be limited to its use as a respiratory stimulant for the collateral excretion of carbon monoxide and industrial contaminants such as Trilene, in patients with normal respiratory and cardiovascular systems.

In patients with respiratory abnormalities the use of carbon dioxide could be dangerous. In respiratory obstruction carbon dioxide induced hyperventilation, could raise the already large intrapulmonary pressure and lead to fluid entering the alveoli with the onset of pulmonary oedema. This applied also in cardiac disease and pulmonary infection. Collapse of the lung could be worsened as the obstructive plug is only drawn deeper into the affected segment.

In emphysema chronic carbon dioxide retention exists. If the emphysematous patient, with acute respiratory infection or cardiac failure, is given oxygen the anoxia is relieved, thus removing the stimulus to respiration and so a fall in ventilation rate occurs. This leads to further carbon dioxide retention and coma follows. The coma is caused by reduced neurone oxygenation by an upset of the enzyme mechanism by either acidosis or the carbon dioxide itself or both. The problem is whether the patient is better alert and anoxic or comatose and oxygenated. The answer seemed to be to give oxygen only in amounts sufficient to raise blood saturation to safe levels and hope that time and renal excretion of acids would allow the patient's respiratory control to adjust itself. An efficient patient-cycled respirator would allow ventilation with adequate oxygenation.

FACULTY NEWS

The following are the names of the 23 candidates who were successful in their examination for the Diploma of Fellow in the Faculty of Anaesthetists, Royal College of Surgeons of England:

Ainley-Walker, J. C. S.
Anderson, J. L.
Brandstater, B. J.
Burkinshaw, Daphne
D'Bras, B. E. G.
Delaney, E. J.
French, O. H.
Genever, R. J.
Jolley, C. R.
Kaufman, L.
Keen, R. L.
Laurie Smith, N.
Lumb, Patricia Mary
Marshall, M.
Merrifield, A. J.
Parker, Sheila Margaret
Phillips, A. H.
Poon, Yee Kit
Prince-White, Freda Elizabeth
Rolfe, M. G.
Schooling, Isabel Brenda
Sims, A. J.
Thomson, T.
Webster, A. C.
Wise, R. P.
Wright, D. G. R.
Young, T. M.

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